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MAY, 1921

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2.

QUANTITATIVE PATHOLOGICAL STUDIES WITH ARSENIC COMPOUNDS

Biological
& Medical
Serials

By

CHARLES W. HOOPER, ALFRED C. KOLLS
and K. DOROTHY WRIGHT

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QUANTITATIVE PATHOLOGICAL STUDIES WITH ARSENIC COMPOUNDS.

I. THE INFLUENCE OF FASTING AND VARIOUS DIETS ON ARSPHENAMINE POISONING, AND THE COMPARATIVE TOXICITY OF ARSPHENAMINE, NEOARSPHENAMINE AND PARA-OXY-META-AMINO-PHENYL-ARSENOXIDE.

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[Submitted for publication February 28, 1921.]

Introduction.

The quantitative studies in chemotherapy published, and in progress by Prof. Carl Voegtlin and his collaborators (1920 and 1921) dealing with the trypanocidal action of antimony and arsenic compounds stimulated the following quantitative pathological studies with arsenic compounds. This is the first paper of a series which will deal with the quantitative action of various drugs on the tissues of the host under varying conditions. It will be seen from this paper that fasting and various diets markedly influence the lesions produced by the intravenous administration of sodium arsphenamine. The action of arsphenamine and neoarsphenamine upon the animal organism differs greatly when considered from a pathological point of view. The kidney lesions produced by arsphenamine, neoarsphenamine, and p-oxy-m-amino-phenyl-arsenoxide are described and compared on a quantitative basis. Experiments are included which show the effect of therapeutic doses of mercury on the kidney following toxic doses of disodium arsphenamine. Liver necrosis with jaundice has been produced by the intravenous administration of lethal doses of disodium arsphenamine. Finally, a method is proposed for the standardization of the rat for the biological testing of drugs.

Experiments with Rats.

A. THE INFLUENCE OF FASTING AND VARIOUS DIETS ON THE TOXICITY OF ARSPHENAMINE.

The influence of fasting and diet upon the toxicity of other drugs has suggested to us that these factors may also play an important rôle in arsphenamine and neoarsphenamine poisoning. On account of the considerable variation in the individual susceptibility of animals to arsphenamine poisoning the number of experiments required in order to obtain reliable data on the effects of diet is necessarily very large. For this reason we have used the albino rat and report the results obtained with over 600 animals. It is clearly shown that a diet of white bread, rolled oats and milk, fed in the days preceding the intravenous administration of arsphenamine, exerts a marked protective action against the toxicity of the drug.

The great difference in the individual susceptibility of patients has already stimulated the following clinical observations: Westrope (1916) stated that a milk diet given 24 hours prior to the administration of arsphenamine reduces the toxic effects of the drug to a minimum, and the patients suffer little or no discomfort. Bailey and McKay (1920) observed that patients with toxic jaundice following the administration of neoarsphenamine and mercury may have an increased amount of blood urea, which they attribute to the high protein content of the diet and to the effect of exercise.

An extensive literature has been developed concerning the influence of fasting and diets on the toxicity of drugs. Lo Monaco and Trambusti (1894) found that well-nourished dogs and rabbits were less resistant to phosphorus than poorly nourished animals. It was also observed that the degenerative changes in the liver and kidneys were much more pronounced when the animals received water during the fasting experiments. Mansfeld (1905) carefully reviewed the previous literature on the effects of fasting on the toxicity of drugs, and studied the influence of inanition on narcosis. He found that starving rabbits were more susceptible to chloral hydrate, paraldehyde, and morphine than were well-nourished animals. On the other hand, the toxic effect of ethyl alcohol, amylene hydrate, and ethyl urethane was not increased by starvation. Ellinger (1905) observed that rabbits fed on oats and given cantharidin subcutaneously showed a severe hemorrhagic nephritis, evidenced by bloody urine and a marked albuminuria. The reaction of the urine was invariably acid. Rabbits fed on turnips and given the same amount of cantharidin subcutaneously showed only a faint trace of albumen, if any, and the reaction of the urine was always alkaline. Beddard (1908) suggested the therapeutic use of dextrose in the treatment of chloroform necrosis, and also the advisability of feeding it before chloroform anæsthesia. His suggestion is based upon Rosenfeld's view that the poisoned liver cells can utilize carbohydrates far better than proteins or fats. Wells (1908) states that feeding of dextrose to animals lessens the amount of fatty degeneration which results from phosphorus poisoning, and presumably it should have some similar effect in chloroform poisoning. Foster (1910) studied the influence of different proportions of protein in the food on resistance to the toxicity of ricin and on recuperation from hemorrhage. He considered the ricin experiments inconclusive and that recuperation from hemorrhage depends more upon the breed of the dog and individual idiosyncrasy than upon the amount of protein in the diet.

Salant and Rieger (1910) studied the effect of starvation on the toxicity of caffein. The fatal dose for rabbits starved four or five days was about 30 per cent less than for well fed animals. Hunt (1910) made careful observations on the effects of a restricted diet and of various diets upon the resistance of animals to certain poisons. The most striking results were obtained with acetonitrile. Guinea pigs and mice kept upon a restricted diet were more resistant to acetonitrile than those kept on an unrestricted diet. Mice, fed upon articles of food such as enter largely into the daily diet of man, varied greatly in their resistance. He was able to alter the resistance of the animals at will and to overcome the effects of one diet by combining it with another. The protective action is attributed by Hunt, in part, to a specific effect upon the thyroids. Dextrose, oatmeal, liver and kidney increased the resistance while eggs, milk, cheese and various fats greatly lowered the resistance. Several glands, notably prostate and testes exerted a beneficial effect similar to but much less marked than that of thyroid, while thymus, parathyroids and suprarenals had either no effect, or an effect opposite to that of thyroid. Diet also had a profound effect on propionitrile poisoning. The toxicity of morphine was distinctly but not markedly affected. Salant and Rieger (1912) studied the protective action of diet against the toxicity of caffein. It was found that a high protein diet for the adult dog tended to greater resistance of the animal to caffein, and similarly, the growing dog tolerated larger quantities of caffein on a milk diet than on a diet of meat. Salant and Smith (1914) observed that carrot-fed rabbits resisted much larger doses of sodium tartrate than those which received oats and cabbage. More than twice the fatal dose could be given without producing symptoms. Opie and Alford (1914 and 1915) investigated the influence of diet upon necrosis caused by hepatic and renal poisons. Rats were used as experimental animals. A rich carbohydrate diet, it was found, protects the parenchymatous cells of the liver or kidneys from necrosis caused by chloroform, phosphorus, potassium chromate and uranium nitrate. Chloroform and uranium nitrate were much more toxic to animals which had received a diet consisting in great part of fat than to those which had received meat. The susceptibility to intoxication with phosphorus was not increased by a diet of fat. The toxicity of potassium chromate was not greater after a diet of fat than after a diet of meat.

Graham (1915) demonstrated that the feeding of carbohydrates to adult dogs increases their resistance against liver necrosis by chloroform. Salant and Nelson (1915) found the toxicity of oil of chenopodium for cats and rabbits which had received cottonseed or coconut oil was diminished at least 50 per cent in some cases. Evidence was also obtained that a diet rich in carbohyrates has a similar effect on rabbits to which the essential oil was administered. Salant and Bengis (1917) observed that the administration of the oil of chenopodium by mouth and subcutaneously may be followed by renal disturbances in rabbits fed exclusively on oats. No evidence of impaired kidney function was obtained when the same, or even larger, doses were administered to rabbits on a diet of carrots. Salant and Wise (1918) demonstrated the protective action of diet against zinc malate poisoning. The rabbits which received an exclusive carrot diet exhibited a decidedly greater resistance to zinc poisoning than those which were fed oats alone. The glycosuria and albuminuria were also frequently absent in the carrot-fed rabbits. Salant and Swanson (1918) published further articles on the influence of diet on the toxicity of sodium tartrate and the protective action of diet against tartrate nephritis. Rabbits, cats, and rats were used as experimental animals. The sodium tartrate was administered subcutaneously. The diets arranged in order of their protective value are as follows: For rabbits, carrot leaves, young carrots, sweet potatoes, table beets, sugar beets, winter carrots, cabbage, hay, oats, and glucose. Starved rabbits showed the least resistance. The effect of diet in tartrate poisoning in cats and rats was not constant. Cats showed a decreased resistance when starved. Carbonates increased resistance probably by the neutralization of organic acids in the blood. They concluded that the favorable effects of some diets on the toxicity of tartrates might be due to several factors, among them inhibition of bacterial activity in the intestines, vitamines, or unknown constituents that might be present in some diets. The elimination of phenolsulphonephthalein was decidedly inhibited in rabbits receiving a diet of oats as compared with those on a carrot diet.

Davis and Whipple (1919) published a series of articles on the liver injury effected by chloroform anaesthesia as influenced by fasting, various diets, drugs, and chemical agents. They clearly show that no single theory so far advanced will explain the peculiar protective action of certain food substances against the liver injury of chloroform anaesthesia. And further, that it is a reaction of the liver cells, not of substances circulating in the blood stream. Dogs were used as experimental animals. Maximal liver injury was obtained when the animals were starved or placed on a fat diet. Sugar, and diets rich in carbohydrates when fed in the days preceding chloroform anaesthesia exerted a marked protective action against liver injury. Skeletal muscle and heart muscle had a slight protective action while kidney, liver, and brain exerted a considerable amount of protection. Desiccated thyroid, given alone, or in combination with foods did not modify the expected chloroform injury. Glucose, or cream, given intravenously during chloroform anaesthesia did not modify the effect of the drug on a starved animal. Epinephrin, given either subcutaneously or intramuscularly, and quinine sulphate when administered in the days preceding chloroform exerted a marked protective action against liver injury. They point out that these facts should not be lost sight of in the management of human cases in which chloroform is indicated. They recommend liberal amounts of carbohydrates and milk for at least two days preceding the anaesthesia and emphasize the fact that it is dangerous to give chloroform to man or animal whenever a fasting period has preceded the administration of the anaesthetic. Voegtlin, Hooper and Johnson (1920) published experiments which seem to indicate that dogs on a mixed or meat diet are more resistant to trinitrotoluene poisoning than animals fed on bread and milk. The animals fed on bread and milk as a rule showed a more acute and severe anaemia and died sooner.

EXPERIMENTAL.

Approximately all the deaths due to arsphenamine poisoning in rats occur within two days after the injection. Many of the animals die within 12 hours and show a characteristic pathological picture. The lungs are usually distended, congested, oedematous and may contain petechiae. The right heart is dilated. The liver, spleen, kidneys and the mucosa of the small intestine are usually engorged. Frequent interstitial hemorrhages are also found in the kidneys. The most characteristic and constant pathological finding in rats that die on the second day is the necrosis of the epithelial lining of the uriniferous tubules. Central hyaline necrosis of the liver lobules may occur but this is extremely rare (only 10 animals in over 600 injected). The detailed pathological findings will be described later and compared with those found in animals poisoned with neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide.

Tables A, B, and C briefly summarize the results obtained in the feeding and fasting experiments. Table A shows the percentage of rats that died within two days, Table B shows the percentage of rats that died acutely within 12 hours, and Table C shows the percentage of rats that lived 12 hours or longer and showed kidney necrosis. In order to place the experiments on a quantitative basis, the doses given in the tables represent the number of cubic centimeters of a 1/100 arsenic equivalent solution per kilo body weight. Ten c. c. 1/100 arsenic equivalent solution contained 24.88 mg. arsphenamine. From 9 to 43 rats were injected with each dose given in the tables. Careful necropsies were made on all the animals and the tissues sectioned and stained. The bread, rolled oats and milk diet contained approximately 65 percent carbohydrate, 22 per cent protein, and 13 per cent fat. The lean beef heart diet contained approximately 90 per cent protein and 10 per cent fat. The rats on the 40 per cent saccharose solution consumed from 12 to 15 c. c. daily. For the individual animal protocols, see Appendix Tables 1–25.

TABLE A.—*Arsphenamine (sodium salt) intravenously—The influence of various diets and fasting on its toxicity—Percentage of rats that died.*

[The numbers within the brackets represent the number of rats used in the series.]

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution).								
	10 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*
Three-day fast	12 [17]	9 [23]	20 [10]	....	46 [24]	90 [10]	....	....	....
Three days on 40 per cent saccharose solution	....	32 [28]	59 [27]	....	63 [43]	69 [13]	....	....	....
Six days on lean beef heart	....	0 [10]	0 [15]	0 [14]	42 [26]	48 [25]	50 [20]	100 [10]	....
Six days on bread, rolled oats, and milk	....	0 [15]	0 [13]	0 [9]	0 [15]	37 [19]	60 [20]	89 [18]	100 [10]

TABLE B.—*Arsphenamine (sodium salt) intravenously.—The influence of various diets and fasting on the acute reaction—Percentage of rats that died acutely and within 12 hours after the injection.*

[The numbers within the brackets represent the number of rats used in the series.]

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution).								
	10 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*
Three-day fast	0 [17]	0 [23]	20 [10]	....	37 [24]	70 [10]	....	....	....
Three days on 40 per cent saccharose solution	....	25 [28]	48 [27]	....	54 [43]	69 [13]	....	....	....
Six days on lean beef heart	....	0 [10]	0 [15]	0 [14]	38 [26]	36 [25]	25 [20]	90 [10]	....
Six days on bread, rolled oats, and milk	....	0 [15]	0 [13]	0 [9]	0 [15]	32 [19]	60 [20]	72 [18]	100 [10]

TABLE C.—*Arsphenamine (sodium salt) intravenously—The influence of various diets and fasting on the kidney necrosis—Percentage of rats that lived 12 hours or longer and showed kidney necrosis.*

[The numbers within the brackets represent the number of rats that lived 12 hours or longer. See Table B for the number of rats used in each series.]

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution).								
	10 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*
Three-day fast	0 [17]	0. 9 [23]	50 [8]	....	73 [15]	100 [3]	....	....	....
Three days on 40 per cent saccharose solution	....	19 [21]	93 [14]	....	70 [20]	100 [4]	....	....	....
Six days on lean beef heart	....	0 [10]	0 [15]	50 [14]	63 [16]	88 [16]	93 [15]	100 [1]	....
Six days on bread, rolled oats, and milk	....	0 [15]	16 [13]	22 [9]	20 [15]	16 [13]	88 [8]	80 [5]	....

It is seen from the tables that the animals on a diet of white bread, rolled oats and milk are much more resistant than the rats fed on a diet of lean beef heart. The resistance is markedly lowered by feeding 40 per cent saccharose solution and by fasting. For example, compare the rats that received 40 c. c. 1/100 arsenic equivalent solution per kilo body weight. This represents 100 mg. of the drug per kilo, the amount 60 per cent of the rats are required to tolerate for two days in the official method for testing arsphenamine. All of the rats on a diet of bread, rolled oats and milk survived and only 20 per cent when sacrificed showed kidney necrosis. The necrosis was very slight. (See Appendix Table 11.) Of the rats that received a beef heart diet, 42 per cent of the animals died, 38 per cent with the acute reaction, and 63 per cent showed kidney necrosis. As a rule, from one-fifth to two-thirds of all the kidney tubules were characteristically necrotic. Of the animals that were fasted for three days, 46 per cent died, 37 per cent with the acute reaction, and 73 per cent showed kidney necrosis. The severity of the necrosis was about the same as that of the animals on a beef heart diet. Of the animals that received 40 per cent saccharose solution, 63 per cent of the animals died, 54 per cent with the acute reaction and 70 per cent showed kidney necrosis. The kidney necrosis was extensive and the edema of the lungs most pronounced. In many instances the pleural cavities were filled with fluid.

We do not wish to venture a hypothesis to explain the fact that sugar feeding alone does not protect rats against arsphenamine poisoning.

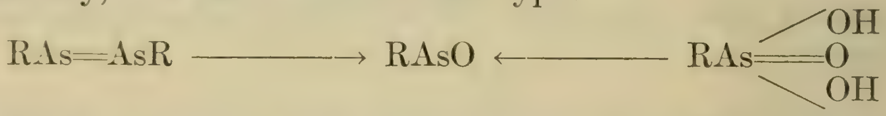
B. STANDARDIZATION OF THE RAT FOR THE BIOLOGICAL TESTING OF DRUGS.

In the official method for testing arsphenamine, it is required that white rats weighing 100 to 150 gm. shall tolerate 100 mg. of the drug per kilo body weight for 48 hours when given intravenously as a 2 per cent alkaline solution, 0.9 c. c. of normal sodium hydrate being used for 100 mg. of arsphenamine. It is further required that the rate of injection shall be 12 to 15 seconds for every 0.1 c. c. of solution. It is also stated in the regulations that the rats should be fed on a well-balanced ration of white bread, cracked corn, cow's milk, and, in addition, twice weekly, fresh beef and cabbage. An adequate supply of fresh, clean water should be provided at all times. The rats should have no access to food for from 18 to 12 hours preceding the injection, though water should be supplied during this time. During the period of observation following the injection, the rats should be fed on the same mixed diet as described above.

We wish to emphasize that accurate diet control is fully as important as the amount of drug which may be tolerated. The mixed diet of white bread, rolled oats and whole milk used in our experiments was in the proportion of 1, 1, to 3. It was thoroughly mushed together in a hashing machine so that the rats were compelled to eat the mixture. The animals were fasted for 17 hours before beginning the diet, when the initial weights were recorded. At the end of six days they were again fasted for from 18 to 22 hours when the final weights were recorded. Fresh water was supplied at all times. The final weights were used for computing the doses of the drug. Young rats weighing between 75 and 125 gm. gain on the average 6 per cent during the six days. If the rats lose weight during the period it is evident that they are pathological and therefore should not be used for testing the drug.

C. THE COMPARATIVE TOXICITY OF ARSPHENAMINE, NEOARSPHENAMINE AND PARA-OXY-META-AMINO-PHENYL-ARSENOXIDE.

Differences in the toxicity of various arsenic preparations have been explained by Voegtlin and Smith (1920) on the hypothesis that they must be changed to one type, namely, the trivalent oxides RAsO before exerting their principle toxic action either upon protozoal parasites or upon the tissues of the host. They have pointed out that the other forms, such as arsenobenzol derivatives, $RAs=AsR$, and pentavalent arsenicals, $RAs(O)(OH)_2$, are without direct injurious action except as they are converted by oxidation or reduction, respectively, into the trivalent oxide type:



$$RAs{=}AsR \longrightarrow RAsO \longleftarrow RAs\begin{array}{l}\diagup OH\\ {=}O\\ \diagdown OH\end{array}$$

Accordingly, p-oxy-m-amino-phenyl-arsenoxide would represent the active trivalent oxide of arsphenamine. Furthermore, it is concluded that the nature and rate of oxidation of arsphenamine and neoarsphenamine to the corresponding oxides furnish an explanation of the increase in toxicity and trypanocidal activity of these compounds, when their solutions are exposed to air.

Ehrlich (1913) observed that the toxicity of a slightly alkaline aqueous solution of arsphenamine or an aqueous solution of neoarsphenamine increases rapidly when kept in contact with air.

Roth (1920), among other things, found that shaking aqueous solutions of neoarsphenamine or alkalinized arsphenamine in the presence of air increases their toxicity markedly. Shaking neoarsphenamine solution with air for 10 minutes increased the toxicity over 400 per cent.

With the above facts in mind, it was decided to compare arsphenamine, neoarsphenamine, and p-oxy-m-amino-phenyl-arsenoxide pathologically on a quantitative basis. The diet was controlled by placing the rats on a diet of bread, rolled oats and milk for six days before making the injections. The animals, 311 in all, were carefully necropsied and tissues sectioned and stained. (See Appendix for other experimental methods.) The individual animal protocols may be found in the Appendix Tables 8 to 15 and 26 to 38.

Necrosis of the kidney parenchyma has been found to be the most constant lesion common to all three drugs and has been used by us to compare the toxicity of the drugs pathologically.

Table D shows clearly that p-oxy-m-amino-phenyl-arsenoxide is by far more toxic to the kidney than either neoarsphenamine or arsphenamine. Arsphenamine is the least toxic of the three drugs when compared on an arsenic equivalent basis. 4 c. c. 1/100 arsenic equivalent solution of p-oxy-m-amino-phenyl-arsenoxide per kilo body weight produces kidney necrosis, while it takes 20 c. c. of neoarsphenamine and 30 c. c. of arsphenamine. It may be said, therefore, that p-oxy-m-amino-phenyl-arsenoxide is five times more toxic to the rat kidney than neoarsphenamine, and seven and one-half times more toxic than arsphenamine. Further, it is shown that neoarsphenamine is 50 per cent more toxic to the rat kidney than arsphenamine. It should also be emphasized that the dose of neoarsphenamine required to cause kidney necrosis in the rat on the ideal diet of bread, rolled oats, and milk is only five times as large as the dose ordinarily used clinically, while the dose of arsphenamine required is almost eight times as large.

Table E gives a clear-cut picture of the death rate of animals on a constant diet. Roth (1920) compared the toxicity of arsphenamine and neoarsphenamine on about 1,400 rats. He observed that approximately all the deaths due to arsphenamine occur within two days after the injection and those from neoarsphenamine within five days. Accordingly, our rats were sacrificed after the periods stated by Roth, so that the pathology of the tissues could be studied.

Table F shows the percentage of rats that died acutely. Usually the acute deaths following the injection of arsphenamine and p-oxy-m-amino-phenyl-arsenoxide were characterized by distention, congestion, edema, and petechiae of the lungs, with dilatation of the right heart, and congestion of the abdominal viscera. The acute deaths following p-oxy-m-amino-phenyl-arsenoxide were also invariably accompanied by a marked increase in the pleural fluid. Following the intravenous injection of neoarsphenamine the acute deaths were associated with severe bleeding from the site of injection or with other inexplicable accidents. There was no distention or edema of the lungs and the pleural fluid was not increased. These results are in harmony with those of Jackson and Smith (1918). These authors conclusively demonstrated by pharmacological experiments

TABLE D.—*Arsphenamine (sodium salt), neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide (sodium salt) intravenously—A quantitative comparison of their toxic effect on the kidney—Rats injected intravenously after six days on bread, rolled oats, and milk—Percentage of rats that lived 12 hours or longer and showed kidney necrosis.*

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution).														
	2 c. c.	4 c. c.	6 c. c.	8 c. c.	10 c. c.	15 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.	80 c. c.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
P-oxy-m-amino-phenyl-arsenoxide	0 [14]	7 [15]	38 [13]	80 [15]	100 [6]	....	....	....	....	....	....	....	....	....	....
Neoarsphenamine	....	....	....	....	....	0 [15]	27 [15]	21 [14]	....	67 [12]	87 [14]	....	100 [14]	90 [21]	100 [15]
Arsphenamine	....	....	....	....	....	....	0 [15]	16 [13]	22 [9]	20 [15]	16 [13]	88 [8]	80 [5]	....	....

The numbers within the brackets represent the number of rats that lived 12 hours or longer. See Table F for the number of rats used in each series.

TABLE E.—*Arsphenamine (sodium salt), neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide (sodium salt) intravenously—A quantitative comparison of their toxicity—Rats injected intravenously after six days on bread, rolled oats, and milk—Percentage of rats that died.*

[The numbers within the brackets represent the number of rats used in the series.]

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution)[1].														
	2 c. c.	4 c. c.	6 c. c.	8 c. c.	10 c. c.	15 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.	80 c. c.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
P-oxy-m-amino-phenyl-arsenoxide	0 [14]	0 [15]	8 [13]	7 [15]	45 [11]	....	....	....	....	....	....	....	....	....	....
Neoarsphenamine	....	....	....	....	....	0 [15]	0 [15]	7 [15]	....	8 [13]	7 [15]	....	7 [15]	14 [21]	7 [15]
Arsphenamine	....	....	....	....	....	....	0 [15]	0 [13]	0 [9]	0 [15]	37 [19]	60 [20]	89 [18]	100 [10]	....

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[1] 10 c. c. 1/100 arsenic equivalent solution contained either 26.78 mg. p-oxy-m-amino-phenyl-arsenoxide, 39.33 mg. neoarsphenamine or 24.88 mg. arsphenamine.

TABLE F.—*Arsphenamine (sodium salt), neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide (sodim salt) intravenously—A quantitative comparison of the acute reactions—Rats injected intravenously after six days on bread, rolled oats, and milk—Percentage of rats that died acutely and within 12 hours after the injection.*

[The numbers within the brackets represent the number of rats used in the series.]

	Dose expressed in c. c. per kilo (1/100 arsenic equivalent solution).														
	2 c. c.	4 c. c.	6 c. c.	8 c. c.	10 c. c.	15 c. c.	20 c. c.	30 c. c.	35 c. c.	40 c. c.	50 c. c.	55 c. c.	60 c. c.	70 c. c.	80 c. c.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
P-oxy-m-amino-phenyl-arsenoxide	0 [14]	0 [15]	0 [13]	0 [15]	45 [11]	....	....	....	....	....	....	....	....	....	....
Neoarsphenamine	....	....	....	....	....	0 [15]	0 [15]	7 [15]	....	8 [13]	7 [15]	....	7 [15]	0 [21]	0 [15]
Arsphenamine	....	....	....	....	....	....	0 [15]	0 [13]	0 [9]	0 [15]	32 [19]	60 [20]	72 [18]	100 [10]	....

on dogs that either acid or alkaline solutions of arsphenamine given intravenously in toxic doses produce a very marked and prolonged rise in the pulmonary blood pressure, a rise that may be 100 per cent above the normal. In a later paper by Smith (1920) it was shown that p-oxy-m-amino-phenyl-arsenoxide affected the pulmonary blood pressure in a manner quite comparable with that of a solution of arsphenamine of corresponding strength. Neoarsphenamine, in the same concentration and the same rate of injection was without effect on the pulmonary blood pressure. Jackson and Raap (1920) have further shown that good preparations of arsphenamine have almost no direct action on the bronchial musculature of the dog.

In conclusion, it should be emphasized that the dose of arsphenamine required to produce the acute lung picture with death in rats on a bread, rolled oats, and milk diet is 12 times greater than the dose used clinically.

D. COMPARISON OF KIDNEY LESIONS PRODUCED BY ARSPHENAMINE, NEOARSPHENAMINE AND PARA-OXY-META-AMINO-PHENYL-ARSENOXIDE.

In general the kidney lesions produced by arsphenamine and neoarsphenamine in rats agree with those described by Pearce and Brown (1915) for dogs and guinea pigs. We have found the lesions produced by p-oxy-m-amino-phenyl-arsenoxide to be of the same general type.

The kidneys of rats that are killed acutely with arsphenamine or p-oxy-m-amino-phenyl-arsenoxide are usually red. Microscopically, the blood vessels are engorged and interstitial hemorrhages are frequent in the boundary zone of the medulla. The kidneys of rats that die after 12 to 24 hours are swollen and show opaque, yellowish-white striations representing tubular necrosis. Microscopically, the essential feature is the tubular necrosis. After a large dose of the drug from one-third to two-thirds of all the kidney tubules may contain necrotic parenchyma cells. The cells are swollen, desquamated, and appear as pink-staining hyaline masses. The nuclei have either disappeared or remain as pycnotic,[1] deeply stained bodies. In many of the tubules the entire epithelium may be destroyed and appear as homogeneous pink-staining, slightly granular masses. The distribution of the tubules containing necrotic cells may be very irregular. Tubules in the outer cortex, inner cortex, and the boundary zone of the medulla may be affected. For p-oxy-m-amino-phenyl-arsenoxide, the most frequent site is the inner cortex and boundary zone of the medulla. Usually the glomeruli are large. The tufts well fill the capsular spaces and do not appear especially abnormal.

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[1] Condensed or reduced in size.

Edema of the labyrinth occurs infrequently. The collecting tubules frequently contain casts.

The changes produced in the kidney by neoarsphenamine are far more severe when compared with those produced by the same arsenic equivalent dose of arsphenamine. In gross, the kidneys are enlarged, swollen, opaque, and pale. Microscopically, the tubular necrosis is the most characteristic feature. Calcification of the necrotic cells is frequent. Here again the distribution of the necrosis may be very irregular, affecting tubules in any portion of the cortex, or the tubules in the boundary zone of the medulla. The glomeruli are usually large. The tufts may well fill the capsular spaces or they may be small and appear compressed by an abundant albuminous precipitate in the capsular spaces. The tuft vessels usually contain endothelial cells and an increased number of polymorphonuclear leucocytes within their lumina. The collecting tubules contain casts.

Experiments with Dogs.

A. KIDNEY LESIONS PRODUCED BY ARSPHENAMINE, NEOARSPHENAMINE—THE INFLUENCE OF MERCURY.

These experiments were undertaken by Dr. Kolls in order to study the influence of various doses of arsphenamine upon the function of the kidneys. The disodium salt of the drug was used for the major portion of the work, but the monosodium salt, the dihydrochloride, as well as neoarsphenamine, were also employed. The dog was chosen as the most desirable species for the experiments. Observations were continued over a considerable period in order to determine the presence or absence of chronic lesions. It was deemed probable that, if conditions could be found under which a degree of renal insufficiency could be produced at will, even if it were temporary, a means would be at hand for the study of the effect of various prophylactic and therapeutic measures upon the course of the lesion. It was also thought important to correlate the observations made with the actual histology of the organ, and to this end the animals were necropsied and the organs studied pathologically. Finally an attempt was made to determine what influence the administration of mercury in various forms and by various routes would have on the course of the lesion. The detailed report of the urine and blood findings will be published later.

In brief it may be said that all the animals receiving 50 mg. disodium arsphenamine per kilo survived. This dose invariably caused albuminuria and the appearance of casts in most instances. The function of the kidneys as judged by the reduction in quantity, the excretion of urea, creatinine and phenolsulphonephthalein was not always impaired, the same animal reacting quite differently to the same dose when repeated. With one exception, all animals receiving 75 to 100 mg. per kilo died (see Appendix, dog protocols 1 to 9). It will be noted from the protocols that where the kidney function is depressed it remains so for only a few days. In no case was the secretion completely suppressed. The doses that proved fatal did not cause any grave immediate change in renal efficiency. The late symptoms of the intoxication are those of profound shock, subnormal temperature, cyanosis, rapid and shallow respiration, low blood pressure, and feeble pulse. Four of the animals developed definite icterus accompanied by extensive central hyaline liver necrosis.

The recoveries from sublethal doses are apparently permanent. Chronic nephritis was not produced in a single instance. The excretion of phenolsulphonephthalein was normal, and the urea of the blood remained at the original level. Albuminuria often persisted, but was due in all probability to the cystitis set up by the daily catheterization. Occasionally a few hyaline casts were seen in the centrifugated specimens. These are of little significance in the urine of the dog. Evans, Wynne, and Whipple (1912) have conclusively demonstrated that catheterization of the dog's bladder is followed by a reflex albuminuria and hyaline casts.

The two animals that received 100 mg. neoarsphenamine per kilo and were sacrificed after three weeks showed a surprising amount of renal disturbance. In both instances a prolonged renal depression followed, and at necropsy the kidneys showed subacute diffuse nephritis (see Appendix, dog protocols 23 and 26).

The administration of mercury in doses corresponding to therapeutic doses in man apparently does not materially increase the severity of the renal injury produced by arsphenamine. Furthermore, the kidney injury produced by toxic doses of mercuric chloride is not greatly influenced by arsphenamine (see Appendix, dog protocols 11, 12, 14, 16, and 18 to 21).

B. LIVER NECROSIS WITH JAUNDICE.

As stated above, four of the dogs receiving disodium arsphenamine intravenously developed definite jaundice accompanied by extensive central liver necrosis (see Appendix, dog protocols 2, 3, 8, and 9). The dogs received a diet of medium fat beef preceding the administration of the arsphenamine. They were given a single dose of from 65 to 100 mg. per kilo and died either on the third or the fifth day following the injection. The necropsies showed extensive central liver necrosis, in some instances comparable with acute yellow atrophy. The livers were swollen and quite fatty in appearance. The capsules were thin. On cross section the lobules were sharply outlined with deep red centers and opaque yellowish-brown peripheries. The gall bladder and bile ducts were normal. Microscopically, there was an extensive central necrosis. From one-third to four-fifths of the liver cells surrounding the efferent veins were killed and appeared as pink-staining hyaline masses. These areas contained a great many wandering cells and red blood cells. The liver cells about the portal areas were swollen and contained many fat droplets (fat stain, osmic acid). The bile ducts were unchanged.

C. MECHANISM OF THE JAUNDICE FOLLOWING THE ADMINISTRATION OF ARSPHENAMINE AND NEOARSPHENAMINE.

We do not wish to enter upon the consideration as to whether the jaundice following the administration of arsphenamine or neoarsphenamine to syphilitic patients is due to the disease or to the drug. We submit experiments on dogs, which show conclusively that arsphenamine itself is capable of causing jaundice with liver necrosis in some instances comparable with acute yellow atrcphy. The type of necrosis is essentially the same as that described for chloroform poisoning by Whipple and Sperry (1909), except that the necrotic areas contain a greater number of red blood cells.

General Summary.

The pathology of experimental arsphenamine, neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide poisoning is described on a quantitative basis.

Starved animals and those fed sugar alone in the days preceding the intravenous administration of sodium arsphenamine are very susceptible to arsphenamine poisoning. A maximal kidney injury is to be expected.

A diet of white bread, rolled oats, and whole milk greatly increases the resistance and exerts a marked protective action against the kidney injury.

A method is proposed for the standardization of the rat for the biological testing of drugs. Accurate diet control in the days preceding the administration of the drug is fully as important as the amount of drug which may be tolerated. Animals unfit for the test may be detected by following the weight curves.

Neoarsphenamine is much more toxic to the rat and dog kidney than sodium arsphenamine. The kidney injury produced by arsphenamine is transient, while that caused by neoarsphenamine may be permanent.

Para-oxy-meta-amino-phenyl-arsenoxide has been found to be five times more toxic to the rat kidney than neoarsphenamine when compared on an arsenic equivalent basis and seven and one-half times more toxic than sodium arsphenamine.

Administration of mercury in doses corresponding to therapeutic doses in man apparently does not materially increase the severity of the renal injury produced by arsphenamine.

Lethal doses of sodium arsphenamine administered intravenously to dogs on a diet of medium fat beef may be followed by jaundice and liver necrosis in some instances comparable with acute yellow atrophy.

Arsphenamine and neoarsphenamine react differently in the animal organism and should not be considered as one and the same compound.

Good preparations of arsphenamine and neoarsphenamine when administered in doses corresponding to those ordinarily used clinically are harmless to the normal animal organism.

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APPENDIX.

1. METHODS USED FOR THE EXPERIMENTS ON RATS.

(*a*) *Compounds of arsenic.*—The arsphenamine (H62 Metz) and the neoarsphenamine (A77 Metz) were commercial preparations which passed the official standard for toxicity at 100 and 200 mg., respectively. The observed arsenic content according to the Lehmann method (1912) was 30.17 per cent for the arsphenamine and 19.07 per cent for the neoarsphenamine. The p-oxy-m-amino-phenyl-arsenoxide was prepared for us by Dr. J. M. Johnson of this laboratory. The observed arsenic content of this compound was 28.0 per cent.

(*b*) *Preparation of solutions.*—Aqueous solutions of the sodium salts were used. The solutions were made up immediately before each experiment in a 10 c. c. volumetric flask with freshly glass-distilled water. Shaking was strictly avoided and as a rule the solutions were used within 30 minutes. The arsphenamine solutions were alkalinized with normal sodium hydrate slightly beyond the clearing point; 1/10 arsenic equivalent solutions of arsphenamine and neoarsphenamine were used for the injections. For the p-oxy-m-amino-phenyl-arsenoxide a 1/50 arsenic equivalent solution was used; 1/10 arsenic equivalent solutions of the arsphenamine and the neoarsphenamine equal 2.49 per cent and 3.93 per cent solutions, respectively. A 1/50 arsenic equivalent solution of "arsenoxide" is equal to a 0.54 per cent solution.

(*c*) *Dose of the drug.*—In order to place the experiments on a quantitative basis the doses given in the tables represent the number of cubic centimeters of a 1/100 arsenic equivalent solution per kilo body weight; 10 c. c. 1/100 arsenic equivalent solution contained 24.88 mg. arsphenamine, 39.33 mg. neoarsphenamine, or 26.78 mg. p-oxy-m-amino-phenyl-arsenoxide.

(*d*) *Method and rate of injection.*—All of the injections were made into the saphenous vein by means of a 1 c. c. syringe accurately graduated to 0.01 c. c. The same syringe was used throughout the entire investigation. The rate of injection was from 12 to 15 seconds for each 0.1 c. c. of solution.

(*e*) *Dietary conditions and care of animals.*—Four series of animals were used for the arsphenamine experiments. The first series was placed on a diet of boiled lean beef heart for six days before the injections. The second series received a diet of white bread, rolled oats, and whole milk in the proportion of 1, 1 to 3. It was thoroughly mushed together in a hashing machine and given for six days before the injections. The third series was given 40 per cent saccharose solution for three days before the injections. The fourth series was fasted for three days before the injections.

The rats that were used for the neoarsphenamine and p-oxy-m-amino-phenyl-arsenoxide experiments received white bread, rolled oats, and milk in the proportions given above for six days before the injections.

In all cases, when the animals were fed, an excess of the diet was provided. An adequate supply of fresh water was given to all the rats except those on 40 per cent saccharose solution.

The animals were kept in metal cages provided with a one-half inch wire mesh floor to prevent the consumption of feces and sawdust.

The weight of the rats varied as a rule from 75 to 125 gm. The rats were fasted for 17 hours before beginning the diet when the initial weights were recorded. They were again fasted for from 18 to 22 hours immediately before the injection when the final weights were recorded. Water was supplied during each of the fast periods. The final weights were used for computing the doses of the drug. The rats on the bread, rolled oats, and milk diet gained on the average 6 per cent, those on beef heart lost 5 per cent, those on 40 per cent sacchrose lost 6.7 per cent, and the rats that were fasted for three days lost 13 per cent. During the period of observation following the injection the rats were fed on the same diet as before.

The rats that received arsphenamine and p-oxy-m-amino-phenyl-arsenoxide were sacrificed after two days. Those that received neoarsphenamine were sacrificed after five days. Careful necropsies were made on all animals.

2. HISTOLOGICAL EXAMINATION OF TISSUES.

For histological detail, the tissues were fixed in Zenker-formalin fluid, washed thoroughly in running water, hardened in alcohol, cut in paraffin, and sections stained with hematoxylin and eosin. The term Zenker-formalin fluid is used to indicate Zenker's fluid without the acetic acid to which 10 per cent of neutral 4 per cent formaldehyde solution is added immediately before use.

For the demonstration of fat, small pieces of tissue were fixed in Müller's fluid, later transferred to Marchi's fluid for five to eight days, washed thoroughly in running water, hardened in alcohol, cut in paraffin, sections cleared in chloroform, and mounted in chloroform balsam.

For the microchemical demonstration of iron, Perl's reaction was employed. Tissues fixed in formalin and cut in paraffin were subjected for 10 minutes to a mixture of a 2 per cent solution of potassium ferrocyanide, one part, and a 1 per cent solution of hydrochloric acid, three parts, heated to 60° C., after which the sections were differentiated in 0.5 per cent hydrochloric acid solution and thoroughly washed in distilled water. The sections were then stained with 0.5 per cent aqueous solution of neutral red for three minutes and counterstained with aqueous eosin.

3. METHODS USED FOR THE EXPERIMENTS ON DOGS.

Medium sized female dogs were used. The diet, unless otherwise noted, was 400 gm. medium fat raw beef and 400 c. c. water daily (water by stomach tube). In one series the water was not controlled. The animals were kept in metabolism cages and the urine collected quantitatively. Two hours before the termination of the 24-hour period 1 c. c. (6 mg.) of phenolsulphonephthalein was injected intramuscularly, a clean bottle placed under the cage and the animal catheterized at the end of two hours. Exactly one-half of the 2-hour specimen during the phthalein excretion period was used for the quantitative estimation of this substance, the other half was combined with exactly one-half of the 22-hour collection for the other procedures. In the earlier experiments the amount of chlorides, urea, and creatinine were also determined. The usual tests for albumen were made and if it occurred in quantity the Esbach quantitative method was employed. The specimens were also examined for bile pigments and casts. The reserve alkalinity of the blood was determined by the method of Marriott (1916), and the urea of the blood by the method described by Folin and Wu (1919).

The arsephenamine and neoarsphenamine solutions were made up from commercial samples which had passed the official biological test for toxicity. The serial number was the same for each preparation. Nine-tenths of a cubic centimeter of normal sodium hydrate was used for each 100 mg. of arsphenamine dihydrochloride for the formation of the disodium salt. The injections were all made into the jugular vein by means of the Woodyatt pump (1917).

[50 mg. disodium arsphenamine, per kilo, intravenously. Three injections at the end of 30, 60, and 218 days after beginning experiment. All injections followed by a period of transient depression of renal function. Chloroformed after 233 days. Necropsy entirely negative.]

Dog 1.—Adult tan and white terrier, weight 9.6 kilos.

February 17, 1919.—Observations begun. Dog is in good state of nutrition. Some nasal discharge. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

March 19.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Animal vomited small amount of bile-stained fluid. A marked depression of renal function resulted, which became evident on the day following the injection and lasted for six days. Bile pigments were present in the urine on the first day. No icterus. Urine contained a small amount of albumen and a few casts.

March 29.—Animal apparently normal. No icterus. Urine contains a few casts and a small amount of albumen. Observations discontinued.

May 13.—Animal is in good condition. Weight 11.6 kilos. Placed on 400 gm. lean beef and 400 c. c. water daily (water by stomach tube).

May 17.—Disodium arsphenamine 50 mg. per kilo, intravenously. Same preparation and technique as above. Vomited at end of injection. Urine contained increased amount of albumen on the second day. Recovery uneventful.

May 31.—Dog is apparently normal. Observations discontinued.

July 3–31.—Nothing of note except a tendency toward albuminuria.

September 3.—Animal has shown some loss of weight in the past month, otherwise normal. Water given ad libitum during this period.

September 11.—Disodium arsphenamine 50 mg. per kilo, intravenously. Same preparation and technique as above. Followed by depression of renal function for one day only. A tendency toward albuminuria for two weeks. Casts were not increased in number.

October 2.—Animal is apparently normal. Weight 9.6 kilos. Urine contains only a trace of albumen and occasional hyaline casts. Phenolsulphonephthalein output is over 60 per cent in two hours. Blood urea determinations do not indicate retention.

October 6.—Dog in excellent condition. Weight 9.4 kilos. Killed with chloroform.

Necropsy.—Animal is well nourished. No icterus. Subcutaneous fat is normal in color. *Thyroids* are normal in gross and in sections. The serous cavities are normal. *Heart* and *lungs* are normal. *Spleen* is normal in gross. Microscopically the pulp contains a few phagocytes loaded with a coarsely granular yellowish-brown pigment. *Stomach* and *intestines* are normal. *Liver* is normal in size. On section the centers of the lobules are somewhat opaque and yellowish-brown in color, the peripheries are translucent reddish-brown. Microscopically the liver cells immediately surrounding the central veins and composing the inner two-thirds of every liver lobule are filled with large and small fat droplets (fat stain, osmic acid). The bile ducts are unchanged. *Pancreas* is normal. Adrenals are normal and show a normal fat distribution (fat stain, osmic acid). Kidneys appear normal in gross. The medullary rays are conspicuous. Microscopically the labyrinth contains an abundance of normal glomeruli. A few have been partially or completely obliterated by fibroblasts and wandering cells. Small irregular patches of fibroblasts are scattered through the boundary zone of the medulla and cortex. The tubules are normal. The tubules in the medullary rays contain a great deal of fat (fat stain, osmic acid). No casts are seen.

[75 mg. disodium arsphenamine, per kilo, intravenously. One injection only. Followed by marked renal depression and definite jaundice. Death on third day. Necropsy showed liver necrosis comparable with acute yellow atrophy, hemorrhagic adrenals containing focal necroses, acute splenic tumor with focal necroses, cloudy swelling of kidneys and bronchopneumonia.]

DOG 2.—Adult black mongrel, female, weight 13.2 kilos.

March 1, 1919.—Excellent condition. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

March 13.—Disodium arsphenamine 75 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Nauseated at end of injection. A small amount of bloody urine passed at end of two hours.

March 14.—Animal depressed and weak. Urine is large in volume. It contains bile pigment, a large quantity of albumen, numerous casts, and red blood cells. Normal constituents are not decreased.

March 15.—Dog is moribund. Definite icterus. Urine is small in volume. All normal constituents are decreased. Albumen, red blood cells, casts, and bile pigments are present. Weight 12.6 kilos.

Necropsy.—Dog is well nourished. Conjunctivae and mucous membranes of mouth are jaundiced. Subcutaneous fat shows increased pigmentation. Serous cavities are normal. Intima of the aorta is lemon-yellow in color. Oesophagus and trachea are normal. Heart is normal in gross and in sections. *Lungs* show a few small patches of bronchopneumonia and a few small hemorrhagic areas 2 to 4 mm. in diameter. Stomach is normal. The mucosa of the duodenum and jejunum is swollen and markedly congested. Pancreas is slightly congested. *Spleen* is swollen and congested. The capsule is tense. On section the capsule bulges, and the pulp is velvety and deep red. Microscopically the pulp is engorged and contains many small areas of focal necrosis which are indicated chiefly by the accumulation of polymorphonuclear leucocytes and cell débris. *Adrenals* are swollen, congested, and hemorrhagic. Microscopically the vessels of both the cortex and medulla are dilated and filled with blood. The inner half of the cortex and the medulla are distorted by hemorrhages. There are many focal areas of necrosis in the lower third of the zona fasciculata and zona reticularis, indicated chiefly by nuclear fragmentation and the accumulation of polyblasts. No mitoses are seen. *Kidneys* are swollen. The boundary zone of the medulla and the cortex are somewhat congested. Microscopically the glomeruli are large. The tufts almost fill the capsular spaces, and some may contain endothelial cells within their lumina. The tubular epithelium is swollen and granular, but shows no definite necrosis. Some of the collecting tubules contain red cells. No casts are seen. *Liver* is swollen, pale, and friable. On section the lobules are sharply outlined with a deep red center and opaque yellowish-brown periphery. The gall bladder and bile ducts are normal. Microscopically there is an extensive central necrosis. From one-third to four-fifths of all the liver cells have been killed and appear as pink-staining hyaline masses. These areas contain a great many wandering cells and red blood cells. The liver cells about the portal areas are swollen and contain many fat droplets. No mitoses are seen. The bile ducts are unchanged. Uterus tubes and ovaries are normal. Brain and spinal cord normal.

[75 mg. disodium arsphenamine, per kilo, intravenously. One injection only. Followed by definite jaundice and death on the third day. Necropsy showed extensive liver necrosis, acute nephritis with tubular necrosis, subendocardial hemorrhages and a hemorrhagic thymus.]

Dog 3.—Young yellow and white shepherd, female, weight 12 kilos.

March 1, 1919.—Placed on 400 gm. beef and 400 c. c. water daily (water by stomach tube).

March 15.—Disodium arsphenamine 75 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Depressed at end of injection.

March 16.—Depressed and weak. Staggers. Conjunctivae and skin definitely jaundiced. Rectal temperature 36.2° C. Drawn blood very dark. Pulse weak and irregular, 148 per minute. Respirations 28 to 32 per minute.

March 17.—Found dead and stiff.

Necropsy.—Animal is very well nourished. Definite icterus. The serous cavities are normal. Thymus contains many small hemorrhagic areas 1 to 4 mm. in diameter. Microscopically the hemorrhagic areas contain numerous wandering cells. There are many large mononuclear macrophages loaded with cell fragments. Lungs are voluminous, the lower right lobe is very edematous. Microscopically the alveoli are filled with precipitated fluid. *Heart* shows several small subendocardial hemorrhages in left ventricle. Intima of aorta is lemon yellow. The mucosa of duodenum and jejunum is swollen and congested. *Pancreas* is normal in gross and in section. *Spleen* is swollen. Capsule is tense. Pulp is deep-red and velvety. Microscopically the Malpighian corpuscles are prominent. The pulp is engorged and contains several phagocytes loaded with a granular yellowish-brown pigment. Adrenals are soft and show considerable post-mortem degeneration. Microscopically the vessels of the inner cortex and medulla are dilated and filled with red cells.

Kidneys are swollen and congested. The boundary zone of the medulla is dark-red and contains many opaque tubules extending out into the medullary striae. Microscopically the glomeruli are large and somewhat irregular. The tufts fill about three-fourths of the capsular spaces and are not abnormally distended. Some of their lumina may contain endothelial cells. The capsular spaces are clear. The inner cortex and boundary zone of the medulla contain a few small scattered interstitial hemorrhages. Some of the tubules contain red cells and casts. The tubules within the medullary striae contain considerable fat (osmic acid). The tubular epithelium is swollen and granular. Many of the tubular cells in the labyrinth, medullary striae, and especially in the boundary zone of the medulla are necrotic. These cells are swollen, desquamated, and occasionally hyaline. The nuclei have disappeared or remain as pycnotic, deeply stained bodies. No mitoses are seen. *Liver* is swollen and quite fatty-looking. On section the lobules are conspicuously outlined with a deep-red center and an opaque yellowish-brown margin. The gall bladder and bile ducts are normal. Microscopically the central hyaline necrosis involves from one-third to four-fifths of every liver lobule. The necrotic areas contain a great many red cells and polyblasts. The liver cells appear as hyaline masses and contain a few small fat droplets. The parenchyma cells about the portal areas are swollen and contain many large and small fat droplets (fat stain, osmic acid). No mitoses are seen The bile ducts are unchanged.

[50 mg. disodium arsphenamine, per kilo, intravenously. Two injections at the end of 6 and 68 days after beginning experiment. First injection followed by a transient depression of renal function. Sacrificed after 135 days. Necropsy entirely negative.]

Dog 4.—Adult black and white bull mongrel, female, weight 11 kilos.

March 16, 1919.—Observations begun. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

March 21.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. No immediate reaction.

March 22.—Urine reduced in volume and normal constituents. It contains considerable albumen, bile pigments, and a few granular casts.

April 23.—Renal function has been normal since March 23. Bile pigments were present in the urine for three days. Urine now contains only a trace of albumen and rarely a hyaline cast.

May 23.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 3 c. c. per minute. No immediate reaction. Little or no renal disturbance. Bile pigment tests positive for two days.

May 31.—Observations discontinued. Animal normal.

July 29.—Sacrificed with chloroform.

Necropsy.—Dog is well nourished. No icterus. Serous cavities are normal. Heart, lungs, stomach, intestines, spleen, and pancreas are normal in gross and in sections. *Adrenals* are normal. Fat distribution normal (fat stain, osmic acid). *Kidneys* appear normal. The medullary striae are opaque and yellowish. Microscopically the straight tubules in the medullary striae contain fat (fat stain, osmic acid). Some of the glomeruli have been partially or completely obliterated. A few small irregular patches of scar tissue are scattered through the cortex and medulla. Some of the epithelial cells of the convoluted tubules contain small globules of refractive hyaline material. *Liver* is normal and shows no scarring. Gall bladder and bile ducts normal.

[60 mg. and 50 mg. disodium arsphenamine, per kilo, intravenously, at the end of 6 and 62 days after beginning experiment. Both injections followed by a period of transient depression of renal function. Sacrificed after 108 days. Necropsy negative.]

Dog 5.—Black cocker spaniel, weight 9 kilos.

March 16, 1919.—Observations begun. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

March 21.—Disodium arsphenamine 60 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Animal vomited after the injection. A slight depression of renal function was noted on the fifth day after the injection. Albumen and casts were also present.

March 29.—Observations discontinued. Urine contains occasional casts and albumen persists in traces.

May 12.—Observations begun again. General conditions the same as above.

May 17.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Marked depression of renal function for seven days.

May 31.—Discharged as normal.

July 2.—Sacrificed with chloroform.

Necropsy.—Dog in excellent condition. No icterus. Heart, lungs, stomach, intestines, spleen, and pancreas are normal. *Adrenals* are normal in gross and in sections. *Kidneys* are normal. The medullary striae are rather opaque and yellowish. Microscopically the tubules within the medullary striae contain considerable fat. The glomeruli are normal. No scars. *Liver* is normal. Gall bladder and bile ducts are unchanged.

[Four injections of disodium arsphenamine 100 mg., 50 mg., 50 mg., and 100 mg. per kilo, intravenously, at the end of 9, 28, 39, and 100 days after beginning experiment. Very little depression of renal function after first three injections. Fourth injection was immediately followed by a severe reaction and the animal died during night. Necropsy showed congestion and slight edema of lungs and extreme congestion of abdominal viscera.]

Dog 6.—Tan mongrel, female, weight 8.3 kilos.

April 19, 1919.—Observations begun. Placed on 150 gm. medium fat beef, 150 gm. dog biscuit, 150 gm. milk powder, and 280 c. c. water daily.

April 28.—Disodium arsphenamine 100 mg. per kilo, intravenously. Two per cent solution, rate 2 c. c. per minute. No renal disturbance except the appearance of albumen and casts.

May 17.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Very little reaction. Renal function only slightly depressed.

May 28.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Again very little reaction and very slight effect on kidneys.

May 31.—Discontinued temporarily.

July 3.—Observations resumed. Urine contains a small amount of albumen as a constant finding.

July 28.—Animal in excellent condition. Weight 10 kilos. Disodium arsphenamine 100 mg. per kilo, intravenously. Two per cent solution, rate 2 c. c. per minute. Followed by severe reaction. Died during night.

Necropsy.—Dog is well nourished. No icterus. No increase in pleural fluid. Right heart is dilated and filled with a firm clot. Lungs are congested and slightly edematous in posterior portions. No hemorrhages. The mucosa of entire gastro-intestinal tract is swollen and congested. The mucosa of the duodenum and jejunum is deep red and shows many submucous hemorrhages. The intestinal contents contain blood. Spleen is enlarged. Capsule is tense. The cut section is deep purplish-red and velvety. Microscopically the Malpighian corpuscles are prominent. The pulp is engorged and contains many pigmented phagocytes. Pancreas is congested. Adrenals are soft and show considerable post-mortem change. *Kidneys* are swollen and markedly congested, the capsule strips readily leaving a smooth surface. The cortex and medulla are very dark red (almost purple). Microscopically the vessels of the cortex and medulla are distended with red cells. There are many patches of hemorrhages in the outer cortex and the boundary zone of the medulla. Many of the tubules contain red cells. The glomeruli are large with distended tufts. Some of the tuft lumina contain endothelial cells and hyaline thrombi. Almost all the capsular spaces contain an albuminous precipitate. There is a rather extensive edema of the labyrinth. The tubular epithelium is swollen and very granular, but shows no definite necrosis. *Liver* is swollen and congested. Gall bladder and bile ducts are normal. Microscopically the vessels are dilated and filled with blood. The liver cells are swollen and granular and show no necrosis. Central nervous system shows no change in gross except a slight congestion of vessels of pia.

[50 mg. disodium arsphenamine per kilo, intravenously, at the end of 10, 40, and 94 days after beginning experiment. First injection followed by a moderate depression of renal function. No depression following the second injection. 30 mg. monosodium arsphenamine per kilo, intravenously, at the end of 146 days, followed by a prolonged period of renal depression. Sacrificed on the 170th day. Necropsy negative.]

Dog 7.—Adult white bull mongrel, female, weight 14.8 kilos.

April 19, 1919.—Excellent condition. Placed on a diet consisting of lean beef 150 gm., dog biscuit 150 gm., milk powder 60 gm., and water 80 c. c. In addition to the fluid above the animal received 200 c. c. water daily by stomach tube.

April 29.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Injection followed by retching and vomiting of a small amount of bile-stained fluid. Urine contained bile pigments, albumen, and casts on the following day. On the fourth day distinct evidence of renal impairment became evident, water chlorides, urea, and creatinine were all reduced. This condition persisted for three days, and on the fourth day there was polyuria with marked improvement of creatinine and urea excretion. Albuminuria and cylindruria persisted for nearly two weeks. Recovery was apparently complete except for a trace of albumen which was always demonstrable in the urine.

May 30.—Disodium arsphenamine 50 mg. per kilo, intravenously. Same preparation and technique. No urinary observations.

July 3.—Placed on 400 gm. of medium fat beef daily and 400 c. c. water by stomach tube. Phenolsulphonephthalein alone was followed in the urine.

July 22.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 4 c. c. per minute. No marked effect in daily quantity of urine or in phthalein excretion resulted. However, a marked albuminuria and cylindruria appeared.

August 1.—Observations discontinued.

September 3.—Placed on 400 gm. medium fat beef. Water *ad libitum.* Phthalein and urea determined.

September 12.—Monosodium arsphenamine 30 mg. per kilo, intravenously. One per cent solution, rate 4 c. c. per minute. Moderate depression of renal function on the following day, most pronounced on the third day. The urine volume, urea, and phthalein excretion were diminished. Recovery was prolonged and phthalein excretion continued low until sacrifice of animal.

October 6.—Good condition. Weight 18 kilos. Chloroformed.

Necropsy.—No icterus. The subcutaneous fat is abundant and of normal color. Serous surfaces are normal. Heart and lungs are normal in gross and in section. Gastro-intestinal tract, pancreas, and spleen are normal. *Adrenals* are normal. Microscopically the cortex and medulla are sharply divided by a thin layer of connective tissue. Fat distribution is normal. *Kidneys* appear normal. The medullary rays contain many yellowish striations. Microscopically the glomeruli, in general, are large and normal. Some show a proliferation of the capsular epithelium. A few of the glomeruli have been partially or completely obliterated. The cortex and medulla contain a few small scattered scars. The tubular epithelium within the medullary striae contains large amounts of fat (fat stain, osmic acid). *Liver* is normal in gross, and in sections. The parenchyma cells contain many large and small fat droplets (fat stain, osmic acid).

[100 mg. disodium arsphenamine per kilo, intravenously. One injection only. Followed by a marked renal depression, jaundice, and death on the third day. Necropsy showed extensive liver necrosis, acute nephritis with tubular necrosis, hemorrhagic adrenals, petechiae and slight edema of lungs.]

Dog 8.—Adult short-haired mongrel, female, weight 13 kilos.

April 19, 1919.—Apparently normal. Placed on lean beef 150 gm., dog biscuit 150 gm., milk powder 60 gm., and water 80 c. c. Additional 200 c. c. water daily by stomach tube.

May 2.—Disodium arsphenamine 100 mg. per kilo, intravenously. Two per cent solution, rate 2 c. c. per minute. Volume of urine increased on first day, urea reduced. Volume normal on second day, urea and creatinine markedly reduced. Bile pigments, a large amount of albumen, and many casts were present. Rectal temperature subnormal. Pulse feeble and pressure low. Mucous membranes definitely cyanotic. Conjunctivae slightly jaundiced.

May 4.—Found dead.

Necropsy.—Definite icterus. Subcutaneous fat is abundant and stained yellow. Serous cavities are normal. Heart is normal. *Lungs* are voluminous, slightly edematous and contain many small hemorrhages. Trachea contains a small amount of pink, frothy fluid. Mucosa of duodenum and jejunum are moderately congested. Pancreas is slightly congested. *Spleen* is swollen. Capsule is tense, pulp is deep red and velvety. *Adrenals* are swollen, the medulla is dark red. Microscopically the vessels of the inner cortex and medulla are distended with red cells. The medulla is distorted by hemorrhages. The zona fasciculata contains a strikingly decreased amount of fat (fat stain, osmic acid). No mitoses or necrotic cells are seen. *Kidneys* are scarred, swollen, and congested. Microscopically there are several old scars in the cortex and medulla. The blood vessels of the cortex, and especially those in the boundary zone of the medulla, are dilated and filled with red cells. Small hemorrhages are frequent. Considerable edema of labyrinth. The glomeruli are large. Their tufts are distended with blood, and many contain endothelial cells within their lumina. Some of the capsular spaces contain an albuminous precipitate. The tubular epithelium is swollen and granular. Many of the tubular cells are necrotic. *Liver* is swollen and congested. On cut section the lobules are sharply defined with a dark red center and a swollen yellowish-brown periphery. The gall bladder and bile ducts are normal. Microscopically the parenchyma shows extensive central necrosis. From one-third to four-fifths of the liver cells are necrotic and appear as pink staining hyaline masses. The areas of necrosis are engorged with red cells and contain many wandering cells. The liver cells about the portal spaces are swollen and contain many large and small fat droplets (fat stain, osmic acid). The bile ducts are normal. No mitoses are seen.

The central nervous system is normal except for congestion of the vessels of the pia.

[65 mg. disodium arsphenamine per kilo, intravenously. One injection only. Followed by depression of renal function, icterus, and death on the fifth day. Necropsy showed acute nephritis with tubular necroses, extensive liver necroses, hemorrhagic adrenals with focal necroses, petechiae, and slight edema of lungs.]

Dog 9.—Young adult white terrier, female, weight 9.2 kilos.

April 19, 1919.—Good condition. Pregnant. Placed on 400 gm. beef and 400 c. c. water daily (water by stomach tube).

April 29.—Disodium arsphenamine 65 mg. per kilo, intravenously. Two per cent solution, rate 2–4 c. c. per minute. Followed by polyuria for three days. Urine of high specific gravity with bile pigments, albumen, and casts present. Urea and creatinine content normal.

May 2.—Animal is depressed and weak. Definite icterus of sclerae and skin. Slight cyanosis. Pulse soft and thready. Rectal temperature 34° C. Weight 9.3 kilos.

May 3.—Found dead.

Necropsy.—Definite icterus. Serous surfaces are smooth. Pleural cavities contain an increased amount of fluid. Heart is normal. *Lungs* are edematous at margins and small hemorrhages are seen on the surface. Microscopically many of the alveoli are filled with coagulated fluid. Some are filled with red cells. There is no accumulation of leucocytes. Stomach, intestines, spleen, and pancreas are normal. *Adrenals* are swollen. The inner half of the cortex is swollen and appears to contain extensive hemorrhages. The medulla is congested. Microscopically the vessels of the inner cortex and medulla are dilated and filled with red cells. The inner half of the cortex is distorted by red cells and contains many areas of necrosis indicated by nuclear fragmentation and the accumulation of polyblasts. No mitoses are seen. The zona fasciculata contains very little fat (fat stain, osmic acid). Kidneys are swollen and congested. Microscopically the blood vessels are distended. The cortex contains small patches of hemorrhage. The tufts of the glomeruli are distended and some contain endothelial cells within their lumina. Some of the capsular spaces contain an albuminous precipitate. In general, the tubular epithelium is swollen and granular. The tubular epithelium, especially in the boundary zone of the medulla and outer cortex, shows extensive necrosis. There is slight edema of the labyrinth. The tubules within the medullary striæ contain fat (fat stain, osmic acid). *Liver* is swollen, friable, and rather pale. The capsule is thin. The lobulation is very distinct. Most of the centers are deep red, the margins are yellowish-brown and not especially abnormal looking. The gall bladder and bile ducts are unchanged. Microscopically the central necrosis is irregular, some of the lobules are scarcely affected while others are almost completely necrotic. The necrotic cells contain small fat droplets (fat stain, osmic acid). The necrotic areas are loaded with polyblasts. The live cells in the nonaffected lobules and about the portal areas of the necrotic lobules contain very few fat droplets. The bile ducts are unchanged.

[20 mg. mercury (gray oil) intramuscularly on eighth day and 50 mg. disodium arsphenamine per kilo, intravenously on ninth day after beginning experiment. Followed by a transient icterus. Died of distemper on the twenty-fourth day. Necropsy showed extensive bronchopneumonia and a few subendocardial hemorrhages.]

Dog 11.—Young adult collie, female, weight 18.7 kilos.

June 4, 1919.—Animal normal. Observations begun. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

June 12.—Gray oil containing 20 mg. mercury intramuscularly in hind leg.

June 13.—Disodium arsphenamine 50 mg. per kilo, intravenously. Two per cent solution, rate 3 c. c. per minute.

June 14.—Animal depressed, refused food. No icterus. Urine small in volume, contained bile pigments, albumen, and casts. Urea excretion reduced, phthalein excretion normal.

June 15.—Conjunctivae slightly jaundiced. Urine contained albumen, casts, and a large amount of bile pigment.

June 17–19.—Slight salivation. Urine contained albumen, casts, but no bile pigments.

June 21.—Distemper.

June 28.—Found dead. Weight 15.1 kilos.

Necropsy.—Dog is fairly well nourished. No icterus. Some excess of pleural fluid. Lungs show extensive bronchopneumonia. Heart shows a few small bright red subendocardial hemorrhages. Stomach, intestines, pancreas, and spleen are normal. Adrenals are normal in gross and in sections. *Kidneys* are swollen and pale. Microscopically the tubular epithelium is swollen and granular and shows no necrosis. No fat (osmic acid). Liver is normal in gross and in section. No scarring. No fat (osmic acid).

[Three injections of disodium arsphenamine 50 mg., 10 mg., and 50 mg. per kilo, intravenously, at the end of 4, 14, and 25 days after beginning experiment. Transient depression of renal function after first injection. 10 mg. mercury (gray oil) intramuscularly at the end of 13 days. Sacrificed on 120th day. Necropsy negative.]

Dog 12.—White bull terrier, female, weight 12.3 kilos.

June 3, 1919.—Observations begun. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

June 7.—Disodium arsphenamine 50 mg. per kilo, intravenously. Two per cent solution, rate 4 c. c. per minute. Depression of renal function on the second and third days. Urine contained albumen, casts, and bile pigments.

June 16.—Gray oil containing 10 mg. mercury, intramuscularly in hind leg.

June 17.—Disodium arsphenamine 10 mg. per kilo, intravenously. One per cent solution, rate 2 c. c. per minute. Renal function unchanged. Urine contained a small amount of albumen and a few casts.

June 28.—Disodium arsphenamine 50 mg. per kilo, intravenously. Renal function unchanged.

September 3–30.—Urine contained a trace of albumen. Phthalein output normal.

October 1.—Killed with chloroform.

Necropsy.—No icterus. Subcutaneous fat abundant and of normal color. Serous cavities normal. Heart and lungs normal. Stomach, intestines, pancreas, spleen, and adrenals are normal. *Kidneys* are normal. The medullary striae are rather opaque and yellowish. Microscopically the tubular epithelium within the medullary striae contains considerable fat (fat stain, osmic acid). There are a few small patches of fibroblasts and mononuclear cells in the boundary zone of the medulla. *Liver* is normal in gross and in sections and shows no scarring.

[1 mg. mercuric chloride and 50 mg. potassium iodide per os, given daily at the end of 11 days after beginning experiment. 50 mg. disodium arsphenamine per kilo, intravenously, at the end of 14 days. Urea and phthalein excretion reduced at the end of 25 days. Sacrificed after 57 days. Necropsy negative.]

Dog 14.—White bull mongrel, female; weight, 9.5 kilos.

June 3, 1919.—Excellent condition. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube).

June 14.—Mercuric chloride 1 mg. and potassium iodide 50 mg. in water, per os, daily.

June 17.—Disodium arsphenamine 50 mg. per kilo, intravenously. Two per cent solution, rate 3 c. c. per minute. Urine contained an increased amount of albumen and casts were present for a few days. Urea and phthalein not reduced.

June 28.—Phthalein and urea excretion reduced.

July 30.—Badly hurt in fight. Killed with chloroform.

Necropsy.—Dog is well nourished. No icterus. Serous surfaces normal. Heart and lungs normal. Stomach, intestines, pancreas, and spleen normal. Adrenals are normal in gross and in section and contain the normal amount of fat (fat stain, osmic acid). *Kidneys* appear normal in gross. The medullary striae are rather opaque and yellowish. Microscopically the sections are normal. The straight tubules within the medullary striae contain a large amount of fat (fat stain, osmic acid). There is no scarring. *Liver* is normal in gross and in sections and shows no scarring. Gall bladder and bile ducts are normal.

[1 mg. mercuric chloride and 50 mg. potassium iodide per os, given daily at the end of 12 days after beginning experiment. 50 mg. disodium arsphenamine per kilo, intravenously, at the end of 54 days. No depression of renal function. Sacrificed after 125 days. Necropsy negative.]

Dog 16.—White short-haired mongrel, female; weight, 11.4 kilos.

June 4, 1919.—Observations begun. Placed on 400 gm. meat and 400 c. c. water daily (water by stomach tube).

June 16.—Mercuric chloride 1 mg. and potassium iodide 50 mg. in water per os, daily.

June 17–July 28.—Phthalein excretion normal. Urine contained a slightly increased amount of albumen and rarely casts.

July 28.—Disodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 4 c. c. per minute. Urine showed an increased amount of albumen and an increased number of casts for three days.

September 3–6.—Urine contains albumen and frequent casts. Urea and phthalein excretion not reduced.

September 7.—Apparently normal. Weight, 10.9 kilos. Chloroformed.

Necropsy.—Entirely negative. Dog is well nourished. No icterus. Serous surfaces are normal. Heart and lungs normal. Stomach and intestines normal. Pancreas, spleen, and adrenals normal in gross and in sections. *Kidneys* are normal in gross and in sections. The straight tubules within the medullary striae contain a small amount of fat (fat stain, osmic acid). *Liver* appears normal though fatty looking. Microscopically the sections are normal. The liver cells contain many large and small fat droplets (osmic acid). Gall bladder and bile ducts are normal.

[15 mg. mercuric chloride per kilo in water, per os, at the end of 12 days after beginning experiment. Followed by a period of marked depression of renal function. 50 mg. disodium arsphenamine per kilo, intravenously at the end of 27 days. Followed by a reduced phthalen excretion. Sacrificed after 103 days. Necropsy showed mild chronic diffuse nephritis.]

Dog 18.—Adult brindle bull mongrel, female, weight 13.9 kilos.

June 26, 1919.—Observations begun. Placed on 400 gm. meat and 400 c. c. water (water by stomach tube).

July 8.—Mercuric chloride 15 mg. per kilo, in water, per os. Followed by vomiting, diarrhea. Phthalein excretion markedly reduced. Urine contained considerable albumen and many casts.

July 23.—Disodium arsephenamine 50 mg. per kilo, 1 per cent solution intravenously. Urine: Good volume, increased amount of albumen, many casts and reduction in phthalein excretion.

September 3.—Phthalein excretion low.

October 7.—Weight 14 kilos. Chloroformed.

Necropsy.—Dog is in good condition. Subcutaneous fat is abundant and normal in color. Serous cavities are quite normal. Heart and lungs are normal. Stomach and intestines are normal. Pancreas and spleen are normal in gross and in sections. Adrenals are normal and show the normal distribution of fat. *Kidneys* show a mild chronic diffuse nephritis. The increase in connective tissue is patchy and most marked in the boundary zone of the medulla. The cortex contains several scattered scars. The glomeruli are well preserved. There has been considerable atrophy and shrinkage of tubules in the scarred areas of the medulla. The tubules within the medullary striae contain considerable fat (fat stain, osmic acid). *Liver* is normal and shows no scarring.

[15 mg. mercuric chloride per kilo in water, per os, at the end of 12 days after beginning experiment. Followed by a period of marked depression of renal function. 50 mg. disodium arsphenamine per kilo, intravenously, at end of 28 days. Followed by a slight reduction in renal function. Sacrificed at end of 72 days. Necropsy negative.]

DOG 19.—Black and tan hound mongrel, female, weight 15 kilos.

June 26, 1919.—Observations begun. Placed on 400 gm. beef and 400 c. c. water daily (water by stomach tube).

July 12.—Mercuric chloride 15 mg. per kilo, in water, per os. Followed by a marked reduction in phthalein excretion. Urine contained considerable albumen and many casts.

July 24.—Disodium arsphenamine 50 mg. per kilo, intravenously. Followed by albuminuria and a slight reduction in phthalein excretion.

September 6.—Chloroformed.

Necropsy.—Dog is well nourished. Serous cavities are normal. Thorax, heart, and lungs normal. Stomach and intestines normal. Pancreas, spleen, and adrenals normal in gross and in sections. *Kidneys* appear normal except for a few scars. Microscopically there is an abundance of normal glomeruli and tubules. There are a few linear scars in the cortex. The cortex and boundary zone of the medulla contain a few small patches of connective tissue and accumulated wandering cells of the mononuclear type. The straight tubules in the medullary striae contain large amounts of fat (fat stain, osmic acid). *Liver* is normal. Gall bladder and bile ducts are normal. Microscopically the liver lobules are uniform and the parenchyma cells are normal. Bile ducts are unchanged.

[5 mg. mercuric chloride per kilo, per os, on the first day, 50 mg. disodium arsphenamine per kilo, intravenously, after 6 days, and 40 mg. monosodium arsphenamine per kilo, intravenously, after 82 days. No immediate depression of renal function after the arsphenamine injections. Sacrificed after 100 days. Necropsy negative.]

DOG 20.—Short-haired mongrel, female, weight 9.5 kilos.

June 25, 1919.—Mercuric chloride 5 mg. per kilo, in water, per os. Placed on 400 gm. medium fat beef and 400 c. c water daily (water by stomach tube).

July 1.—Disodium arsphenamine 50 mg. per kilo, intravenously. On the following day the urine contained bile pigments and an increased amount of albumen. After 4 days phthalein excretion was reduced and remained low for a week.

September 3.—Monosodium arsphenamine 40 mg. per kilo, intravenously. One per cent solution, rate 3 c. c. per minute. Urine contained bile pigments. A marked albuminuria and cylindruria appeared 10 days after injection. Phthalein fluctuated with a tendency downward.

October 4.—Weight 8.8 kilos. Killed with chloroform.

Necropsy.—Entirely negative. Subcutaneous fat is abundant and normal in color. Serous cavities normal. Heart and lungs normal in gross and in sections. Stomach and intestines are normal. Pancreas, spleen, and adrenals are normal in gross and in sections. *Kidneys* are normal. Medullary striae show opaque yellowish striations. Microscopically the sections are normal. The tubules within the medullary striae contain a large amount of fat (fat stain, osmic acid). *Liver* is normal in gross and in sections. Gall bladder and bile ducts are unchanged.

[5 mg. mercuric chloride per os, on the first day, 50 mg. disodium arsphenamine per kilo, intravenously after 5 days. Phthalein excretion low after the mercury only. Sacrificed after 29 days. Necropsy negative.]

Dog 21.—Short-haired mongrel, female, weight 10.8 kilos.

June 25, 1919.—Normal. Placed on 400 gm. medium fat beef and 400 c. c. water daily (water by stomach tube). Mercuric chloride 5 mg. per kilo, in water, per os. Followed by marked albuminuria and cylindruria. Phthalein excretion greatly lowered.

June 30.—Disodium arsphenamine 50 mg. per kilo, intravenously. Urine contained bile pigments on second day. No depression of renal function.

July 24.—Weight 9.6 kilos. Killed with chloroform.

Necropsy.—Dog is well nourished. No icterus. Serous cavities normal. Heart and lungs normal. Stomach and intestines appear normal. Spleen, pancreas, and adrenals are normal in gross and in sections. *Kidneys* are normal. The sections show considerable fat in the straight tubules of the medullary rays. *Liver* is normal in gross and in sections. Gall bladder and bile ducts are unchanged.

[100 mg. neoarsphenamine per kilo, intravenously. Followed by a prolonged renal depression. Sacrificed after 21 days. Necropsy showed subacute diffuse nephritis.

Dog. 23.—Terrier mongrel, female, weight 14 kilos.

September 16, 1919.—Placed on 400 gm. medium fat beef, water *ad libitum.* Neoarsphenamine 100 mg. per kilo, intravenously. Two per cent solution, rate 5 c. c. per minute. Followed by albuminuria and some cylindruria. Polyuria quite marked at first. Phthalein excretion greatly depressed and remained low until sacrifice of animal.

October 7.—Killed with chloroform.

Necropsy.—Subcutaneous fat is abundant and of normal color. Heart and lungs are normal. Stomach and intestines show no change. *Spleen* is normal in gross and in sections. The pulp contains a few hemosiderin-containing phagocytes. Pancreas and adrenals are normal in gross and in sections. *Kidneys* show subacute diffuse nephritis. Microscopically the cortex is scarred with an irregular patchy increase of connective tissue containing an accumulation of wandering cells chiefly of the mononuclear type. Some of the scars are linear and involve two or more of the glomeruli with their tubules. The connective tissue increase is most marked within the boundary zone of the medulla. The vast majority of the glomeruli are well preserved and stand out conspicuously. The tubules within the scarred areas show considerable atrophy and shrinkage. The tubules in the nonaffected areas appear normal. *Liver* is normal in gross and in sections. Gall bladder and bile ducts are unchanged.

[50 mg. monosodium arsphenamine per kilo, intravenously. Severe reaction. Death within 12 hours. Necropsy showed congestion and edema of lungs and extreme congestion of abdominal viscera.]

Dog 24.—Small bull mongrel, female.

September 5, 1919.—Normal. Placed on a medium fat beef diet. Water *ad libitum.* Monosodium arsphenamine 50 mg. per kilo, intravenously. One per cent solution, rate 4 c. c. per minute. Followed by a severe reaction and death within 12 hours.

Necropsy.—Dog is well nourished. No icterus. Pleural cavities contain an increased amount of fluid. Trachea contains considerable frothy fluid. *Lungs* are voluminous, congested, and quite edematous. Microscopically the vessels are dilated and filled with blood. Many of the alveoli are filled with coagulated fluid. Mucosa of small intestine is deep red and congested. Spleen is moderately swollen. Microscopically the pulp is engorged. *Adrenals* are soft and show considerable post mortem autolysis. *Kidneys* are swollen and congested. Microscopically the blood vessels are distended and congested. Patches of hemorrhages are conspicuous in the cortex and boundary zone of the medulla. The glomeruli are large. Their tufts are distended with red cells and well fill the capsular spaces. Some edema of the labyrinth. The epithelium of the tubules is swollen and granular. Some of the tubules contain red cells. The tubules within the medullary striae contain considerable fat (fat stain, osmic acid). *Liver* is congested, otherwise normal.

[5 mg. arsphenamine dihydrochloride per kilo, intravenously. Marked reduction in phthalein excretion for 12 days. Sacrificed after 21 days. Necropsy showed bronchopneumonia.]

DOG 25.—Short-haired mongrel, female, weight 10.3 kilos.

September 5, 1919.—Normal. Placed on meat diet. Water *ad libitum.*

September 16.—Arsphenamine dihydrochloride 5 mg. per kilo, intravenously. One per cent solution. Urine, volume not altered, albumen and casts increased. Phthalein excretion markedly reduced for 12 days.

October 7.—Killed with chloroform.

Necropsy.—Dog is in good condition. No icterus. Heart is normal. *Lungs* contain a few small areas of bronchopneumonia. Stomach, intestines and pancreas are normal. *Spleen* is normal in gross. Microscopically the pulp contains a few phagocytes loaded with coarsely granular light-brown iron-containing pigment. *Adrenals* are normal in gross and in sections. Fat stains show the normal distribution of fat. *Kidneys* are normal. The straight tubules in the medullary rays contain large amounts of fat (fat stain, osmic acid). *Liver* is normal in gross and in sections and shows no scarring.

[100 mg. neoarsphenamine per kilo, intravenously. Followed by prolonged renal depression. Sacrificed after 21 days. Necropsy showed subacute diffuse nephritis.]

DOG 26.—Fox terrier mongrel, female, weight 5.3 kilos.

September 5, 1919.—Observations begun. Placed on a medium fat beef diet. Water *ad libitum.*

September 16.—Neoarsphenamine 100 mg. per kilo, intravenously. Two per cent solution. Followed by marked albuminuria. Phthalein excretion reduced after three days and remained low for eight days.

October 7.—Urine contains a trace of albumen. Phthalein excretion slightly lower than before neoarsphenamine injection. Chloroformed.

Necropsy.—Dog is in good condition. No icterus. No increase in serous fluids. Heart, lungs, pancreas and spleen show no change. Adrenals are normal in gross and in sections. *Kidneys* show a mild subacute diffuse nephritis. The sections show an abundance of normal glomeruli and tubules. There are several partially or completely obliterated glomeruli, a patchy increase of connective tissue in the cortex and a more marked increase of interstitial connective tissue in the boundary zone of the medulla. Many of the collecting tubules contain hyaline casts. *Liver* sections show a definite increase in the periportal connective tissue. Some of the lobules are completely surrounded by a narrow band of fibrous tissue. There is some increase in the number of mononuclear cells about the portal areas and the liver cells about these areas contain many fat droplets (fat stain, osmic acid). The parenchyma cells are normal. The bile ducts are unchanged.

[8 mg. arsphenamine dihydrochloride per kilo intravenously. Followed by prolonged renal depression. Sacrificed after 18 days. Necropsy entirely negative.]

DOG 28.—Bull mongrel, female, weight 13.4 kilos.

September 15, 1919.—Observations begun. Placed on a medium fat beef diet. Water *ad libitum.*

September 19.—Arsphenamine dihydrochloride 8 mg. per kilo, intravenously. Followed by a marked albuminuria and cylindruria. Phthalein excretion reduced on the second day and remained low until animal was sacrificed.

October 7.—Killed with chloroform.

Necropsy.—Entirely negative. No icterus. Lungs, spleen, pancreas, adrenals, kidneys and liver are normal in gross and in sections.

[85 mg. neoarsphenamine per kilo, intravenously. Followed by renal depression. Sacrificed after 4 days. Necropsy showed chronic nephritis and a superimposed acute nephritis with tubular necrosis.]

Dog 29.—Short-haired mongrel, female, weight 12.8 kilos.

October 3, 1919.—Observations begun. Placed upon a medium fat beef diet. Water *ad libitum*.

October 4.—Neoarsphenamine 85 mg. per kilo, intravenously. Followed by a marked albuminuria and reduction in phthalein excretion.

October 8.—Killed with chloroform.

Necropsy.—Dog is in good condition. Serous cavities are normal. Heart, lungs, pancreas and spleen are normal in gross and in sections. Adrenals are normal in gross and in sections. No mitoses are seen. The fat in the zona fasciculata may be slightly decreased (fat stain, osmic acid). *Kidneys* show a mild chronic diffuse nephritis with a superimposed acute tubular nephritis. There are many partially or completely obliterated glomeruli, a patchy increase of connective tissue in the cortex and a more marked increase of interstitial connective tissue in the boundary zone of the medulla. There is an abundance of glomeruli and tubules not affected by the chronic change. The glomeruli are large. The tufts well fill the capsular spaces and do not appear abnormal. Some may contain a few endothelial cells within their lumina. The striking acute change is the irregular necrosis of the epithelium lining the tubules. The necrosis is most marked in the convoluted tubules in the outer half of the cortex. Many of the affected tubules contain living and necrotic cells. In others the entire epithelium has been destroyed and appears as homogeneous, pink-staining, slightly granular masses. The necrotic cells contain no fat. No mitoses are seen. Many of the collecting tubules contain casts. *Liver* is normal in gross and in sections and contains no fat.

[85 mg. neoarsphenamine per kilo, intravenously. No evidence of renal injury in three days. Sacrificed after 4 days. Necropsy showed acute nephritis with tubular necrosis.]

Dog 31.—Short-haired mongrel, female, weight 10 kilos.

October 4, 1919.—Normal. Neoarsphenamine 85 mg. per kilo intravenously. No depression of renal function.

October 8.—Killed with chloroform.

Necropsy.—No icterus. Heart, lungs, spleen, pancreas and liver are normal in gross and in sections. *Adrenals* are normal in gross and in sections. No mitoses are seen. The zona fasciculata may contain a slightly decreased amount of fat. *Kidneys* appear normal in gross. Microscopically the vast majority of the glomeruli with their tubules are normal. However, a few of the convoluted tubules, the ascending limbs of Henle and the loops of Henle contain necrotic epithelial cells. The extent of the injury is very slight as compared with the extensive kidney necrosis of Dog 29. *Liver* is normal in gross and in sections.

TABLE 1.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[20 c. c. 1/100 arsenic equivalent solution or 50 mg. arsphenamine per kilo body weight.]

[Room temperature, 26–27° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Hours.*	*Mins.*						*Per cent.*	
328	96	−17	19	6	None	2 days	Killed	No definite change	No definite change	86	
329	106	−19	19	9	do.	do.	do.	do.	do.	88	
330	85	−20	19	12	do.	do.	do.	do.	do.	79	
331	72	−16	19	15	do.	do.	do.	do.	do.	74	Lung abscesses.
332	87	+ 1	19	17	do.	do.	do.	do.	do.	83	
333	91	+ 2	19	20	do.	do.	do.	do.	do.	85	
2	174	+ 7	22	20	do.	do.	do.	do.	do.	....	Splenic tumor.
334	82	− 2	19	23	do.	do.	do.	do.	do.	92	
335	75	− 4	19	26	do.	do.	do.	do.	do.	75	Lungs contain petechiæ.
6	171	− 5	22	55	do.	do.	do.	do.	do.	....	

All of the rats lived; none showed kidney or liver necrosis.

TABLE 2.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[30 c. c. 1/100 arsenic equivalent solution or 75 mg. arsphenamine per kilo body weight.]

[Room temperature 26–27° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Hours.*	*Mins.*						*Per cent.*	
145	98	− 2	19	4	Slight	2 days	Killed	No definite change	No definite change	82	Several small liver abscesses.
152	97	− 1	20	4	None	do.	do.	do.	do.	96	
146	95	+ 1	19	8	Slight	do.	do.	do.	do.	86	
153	94	− 6	20	8	None	do.	do.	do.	do.	90	
154	114	−12	20	12	do.	do.	do.	do.	do.	93	Lung abscesses and petechiæ.
147	97	−11	19	15	Slight	do.	do.	do.	do.	90	Lung abscesses.
55	109	− 8	18	15	None	do.	do.	do.	do.	84	Lung contains petechiæ.
156	103	− 2	20	16	do.	do.	do.	do.	do.	85	
149	84	− 5	19	19	Slight	do.	do.	do.	do.	75	
157	99	+ 1	20	20	None	do.	do.	do.	do.	86	
151	90	+ 4	19	25	Slight	do.	do.	do.	do.	70	Many small liver abscesses.
64	120	+ 2	18	25	None	do.	do.	do.	do.	84	
66	140	− 3	19	32	do.	do.	do.	do.	do.	81	
9	156	− 1	22	47	do.	do.	do.	do.	do.	....	
67	134	+ 2	20	103	do.	do.	do.	do.	do.	90	

All of the rats lived; none showed kidney or liver necrosis.

TABLE 3.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[35 c. c. 1/100 arsenic equivalent solution or 87 mg. arsphenamine per kilo body weight.]

[Room temperature 26–27° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Hours.*	*Mins.*						*Per cent.*	
140	95	− 1	18	4	Slight	2 days	Killed	No definite change	No definite change	78	Many small liver abscesses.
141	94	− 4	18	9	do	do	do	do	do	78	
107	185	− 8	18	11	do	do	do	Moderate necrosis.	do	89	
142	106	+ 3	18	13	do	do	do	No definite change	do	82	Do.
108	186	− 6	18	15	do	do	do	Moderate necrosis.	do	89	
143	96	− 1	18	18	do	do	do	No definite change	do	76	
110	182	− 8	18	20	do	do	do	Moderate necrosis.	do	92	
144	111	− 1	19	23	do	do	do	No definite change	do	84	
111	178	− 7	18	25	do	do	do	Slight necrosis	do	94	
65	110	− 5	19	50	do	do	do	No definite change	do	82	Lung abscesses.
60	114	− 4	19	55	do	do	do	Moderate necrosis.	do	85	
56	130	−15	19	65	do	do	do	Slight necrosis	Fat, moderate	83	Many of the liver cells contain small fat droplets (fat stain, osmic acid).
36	160	−12	20	85	do	do	do	Moderate necrosis.	No definite change	98	
61	117	− 2	20	130	do	do	do	No definite change	do	83	

All of the rats lived; 50 per cent of these showed kidney necrosis.

TABLE 4.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[40 c. c. 1/100 arsenic equivalent solution or 99 mg. arsphenamine per kilo, body weight.]

[Room temperature 24–27° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Hours.*	*Mins.*						*Per cent.*	
327	100	−7	19	3	Slight	2 days	Killed	No definite change	No definite change	81	
106	172	−7	21	5	None	do	do	Slight necrosis	do	78	Many small liver abscesses.
51	144	−12	19	7	Severe	3 hours	Died	Congestion; hemorrhages.	Congestion	....	Acute lung picture; intestinal mucosa and spleen congested.
109	166	−8	22	11	None	2 days	Killed	Moderate necrosis.	No definite change	93	
49	160	−14	19	17	Severe	3 hours	Died	Congestion; hemorrhages.	Congestion	....	Acute lung picture.
116	156	−6	22	20	Convulsions.	10 minutes	do	do	do	....	Acute lung picture; intestinal mucosa congested.
322	76	−1	18	21	Slight	2 days	Killed	Slight necrosis	No definite change.	87	
323	78	−3	18	24	do	do	do	No definite change.	do	87	
123	136	−3	22	25	Convulsions.	60 minutes.	Died	Congestion; hemorrhages.	Congestion	....	Do.
43	132	−10	19	26	Slight	2 days	Killed	Slight necrosis	No definite change.	81	
324	108	−3	18	27	do	do	do	No definite change.	do	84	
325	109	−8	19	32	do	do	do	do	do	89	Few small liver abscesses.
46	148	−12	19	32	do	do	do	Extensive necrosis	Central necrosis ¼	81	Many small and medium-sized fat droplets in central ⅔ of all liver lobules (fat stain, osmic acid).
326	96	+5	19	36	do	do	do	No definite change.	No definite change.	85	
35	157	−15	19	45	do	do	do	Extensive necrosis	do	95	Small and medium-sized fat droplets in liver cells at periphery of necrotic area (fat stain, osmic acid).
38	132	−11	20	55	do	do	do	do	do	91	Lung abscesses; several small liver abscesses.
8	151	+5	22	65	do	do	do	Moderate necrosis.	do	....	Many small liver abscesses.
551	124	−11	19	4	Severe	3½ hours	Died	Congestion	Congestion	....	Acute lung picture; lung abscesses; liver contains tapeworm cysts.
552	130	−8	19	10	do	1 hour	do	do	do	....	Acute lung picture; intestinal mucosa congested; liver contains tapeworm cysts.
553	122	−3	19	14	Moderate	2 days	Killed	Moderate necrosis; casts.	No definite change.	....	Diarrhea; liver contains many tapeworm cysts.
554	135	−4	19	19	Severe	20 minutes	Died	Congestion	Congestion	....	Acute lung picture; abscesses of lung; mucosa of small intestine congested.
555	118	−9	19	24	Moderate	2 days	Killed	No definite change.	No definite change.	....	Diarrhea; lungs contain petechiae; adrenals hemorrhagic; many small liver abscesses.

556	132	— 4	20	28	Severe	8 hours	Died	Congestion	Congestion		Acute lung picture; adrenals hemorrhagic.
557	126	— 5	20	33	do	do	do	Hemorrhages; casts; congestion.	do		Acute lung picture.
558	130	— 5	20	38	Moderate	52¼ hours	do	Extensive necrosis; casts.	No definite change.		Diarrhea; adrenals hemorrhagic.
559	124	— 5	20	6	Severe	1¼ hours	do	Congestion	Congestion		Acute lung picture; intestinal mucosa congested.

Sixty-two per cent of the rats lived over 12 hours; 63 per cent of these showed kidney necrosis; 6 per cent showed central liver necrosis. In some cases the adrenals were hemorrhagic. The rats that died acutely showed distention, congestion, edema, and petechiae of lungs and congestion of the abdominal viscera. Fifty-eight per cent of the rats lived to be sacrificed.

TABLE 5.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[50 c. c. 1/100 arsenic equivalent solution or 124 mg. arsphenamine per kilo body weight.]

[Room temperature 24–27° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Hours.*	*Mins.*						*Per cent.*	
34	153	−10	22	5	Slight	2 days	Killed	Moderate necrosis.	Many mitoses	90	
113	105	− 8	19	5	Moderate	do.	do.	Slight necrosis	No definite change.	90	
318	77	− 8	18	5	Slight	do.	do.	do.	do.	82	
112	100	− 8	19	6	Severe	29 minutes	Died	Congestion; casts	Congestion		Acute lung picture; intestinal mucosa congested.
319	83	−13	18	9	do.	6 hours	do.	Congestion; hemorrhages.	do.		Acute lung picture with abscesses.
114	132	− 8	20	12	do.	33 minutes	do.	do.	do.		Acute lung picture; intestinal mucosa congested.
115	98	−13	19	12	do.	2 days	Killed	Slight necrosis	No definite change.	81	Adrenals hemorrhagic.
320	66	+ 6	18	13	Slight	do.	do.	No definite change.	do.	80	
118	100	−10	19	16	Severe	49 minutes	Died	Congestion; hemorrhages.	Congestion		Acute lung picture with abscesses; intestinal mucosa congested.
321	82	+ 2	19	18	Slight	2 days	Killed	Moderate necrosis.	No definite change.	87	
119	128	+ 2	20	19	Severe	21 minutes	Died	Congestion; hemorrhages.	Congestion		Acute lung picture; intestinal mucosa congested.
44	108	−15	23	20		18 hours	do.	Moderate necrosis.	No definite change.		Acute lung picture with abscesses.
121	100	− 8	19	22	Moderate	2 days	Killed	No definite change.	do.	73	Few small liver abscesses.
120	110	− 2	20	25	do.	do.	do.	Slight necrosis	do.	82	
37	142	−17	20	65		18 hours	Died	Moderate necrosis.	Congestion		Acute lung picture.
1	155	−11	22	75		19 hours	do.	Slight necrosis	No definite change.		Lung abscesses; few small liver abscesses.
42	135	−15	20	75		2 days	Killed	Severe necrosis	do.	73	
542	128	− 8	18	6	Severe	54 minutes	Died	Congestion	Congestion		Acute lung picture with abscesses; intestinal mucosa congested.
543	126	− 5	18	11	Moderate	2 days	Killed	Slight necrosis; casts.	No definite change.		Diarrhea; lungs edematous.
544	135	− 8	18	15	do.	do.	do.	Moderate necrosis; casts.	do.		Diarrhea; adrenals hemorrhagic.
546	110	− 5	18	25	do.	do.	do.	do.	do.		Diarrhea; adrenals very hemorrhagic.
547	134	− 5	18	30	do.	do.	do.	Extensive necrosis; calcification; casts.	do.		Diarrhea; adrenals hemorrhagic; liver contains tapeworm cysts.
548	116	+ 2	18	36	Severe	41 minutes	Died	Congestion	Congestion		Acute lung picture; intestinal mucosa congested.
549	124	− 5	19	7	do.	28 minutes	do.	do.	do.		Do.
550	118	− 1	19	11	do.	32 minutes	do.	do.	do.		Do.

Sixty-four per cent of the rats lived over 12 hours; 88 per cent of these showed kidney necrosis. In some cases the adrenals were hemorrhagic. All of the rats that died acutely showed distention, congestion, edema, and petechiae of the lungs and congestion of abdominal viscera. Fifty-two per cent of the animals lived to be sacrificed.

TABLE 6.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[55 c. c. 1/100 arsenic equivalent solution or 137 mg. arsphenamine per kilo body weight.]

[Room temperature 24° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
466	124	−8	19	7	Severe	1 hour	Died	Congestion	Congestion	Acute lung picture; intestinal mucosa congested.
467	115	−3	19	11	Moderate	2 days	Killed	Slight necrosis; casts.	No definite change.	
468	120	−2	19	17	do	do	do	Slight necrosis	do	Acute lung picture.
469	128	−2	19	22	do	do	do	do	do	Many small liver abscesses.
470	112	−6	19	26	Severe	3½ hours	Died	Congestion	Congestion	Acute lung picture.
471	122	+3	19	30	Moderate	2 days	Killed	Moderate necrosis.	No definite change.	Lungs contain petechiæ.
472	125	−2	19	34	do	do	do	do	do	Adrenals hemorrhagic.
517	94	−3	19	5	Severe	11 hours	Died	Congestion	Congestion; few hemorrhages.	Pleural fluid increased; acute lung picture; thymus contains petechiæ.
518	90	0	19	9	do	29½ hours	do	Slight necrosis	No definite change.	Acute lung picture.
519	90	+4	19	15	do	22 hours	do	Congestion; casts.	Congestion; hemorrhages.	Pleural fluid increased; acute lung picture; thymus contains petechiæ.
520	96	0	19	21	do	24 hours	do	Slight necrosis; congestion.	do	Acute lung picture; adrenals hemorrhagic.
521	94	+2	19	27	do	12¾ hours	do	Slight necrosis; casts; congestion.	Congestion	Acute lung picture; adrenals hemorrhagic; thymus contains petechiæ; intestinal mucosa congested.
522	94	+3	19	31	do	15¾ hours	do	Slight necrosis; casts.	Congestion; hemorrhages.	Acute lung picture; adrenals hemorrhagic.
524	90	0	19	35	Moderate	2 days	Killed	Moderate necrosis; casts.	No definite change.	Adrenals hemorrhagic.
473	130	−4	19	3	do	do	do	do	do	Lungs show edema and petechiæ; adrenals hemorrhagic.
474	144	−3	19	8	do	do	do	do	do	Adrenals hemorrhagic.
475	136	−1	19	12	do	do	do	do	do	Lungs contain petechiæ; adrenals hemorrhagic; many small liver abscesses.
525	90	+1	19	4	Severe	10½ hours	Died	Congestion	Congestion; hemorrhages.	Pleural fluid increased; acute lung picture; thymus contains petechiæ.
526	102	0	19	9	Moderate	2 days	Killed	Slight necrosis; casts.	No definite change.	
527	89	+1	19	13	Severe	10½ hours	Died	Congestion	Congestion	Acute lung picture; thymus contains petechiæ; intestinal mucosa congested.

Seventy-five per cent of the rats lived over 12 hours; 93 per cent of these showed kidney necrosis. In some instances the adrenals and thymus were hemorrhagic. All of the rats that died acutely showed distention, congestion, edema, and petechiæ of lungs and congestion of the abdominal viscera. The pleural fluid was markedly increased in some. Fifty per cent of the rats lived to be sacrificed.

TABLE 7.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on lean beef heart.*

[60 c. c. 1/100 arsenic equivalent solution or 149 mg. arsphenamine per kilo body weight.]

[Room temperature 28° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
446	168	−6	19	5	Severe	30 minutes	Died	Congestion; hemorrhages.	Congestion	Acute lung picture; acute splenic tumor.
447	150	−7	19	11	do	2¼ hours	do	Congestion	do	Pleural fluid increased; acute lung picture; intestinal mucosa congested.
448	141	−6	19	16	do	19 minutes	do	do	do	Acute lung picture.
449	127	−8	19	21	do	45½ hours	do	Extensive necrosis; congestion; hemorrhage.	No definite change.	Lungs contain petechiæ.
450	122	−7	19	25	do	20 minutes	do	Congestion	Congestion	Acute lung picture; intestinal mucosa congested.
451	152	−5	19	32	do	23 minutes	do	do	do	Do.
452	138	−7	19	36	do	19 minutes	do	do	do	Do.
453	138	−4	20	5	do	22 minutes	do	do	do	Do.
454	134	−6	20	10	do	1 hour	do	do	Congestion; fat+	Do.
455	148	−4	20	15	do	12 minutes	do	do	Congestion	Do.

Ten per cent of the rats lived over 12 hours and showed extensive kidney necrosis; 90 per cent of the rats died within 1 hour with distention, congestion, edema, and petechiæ of lungs and congestion of the abdominal viscera. None of the rats lived to be sacrificed.

TABLE 8.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[20 c. c. 1/100 arsenic equivalent solution or 50 mg. arsphenamine per kilo body weight.]

[Room temperature, 20.5° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
955	72	0	19	3	Slight	2 days	Killed	No definite change.	No definite change.	
956	82	0	19	5	do	do	do	do	do	
957	76	−8	19	7	do	do	do	do	do	Lung abscesses.
958	74	−1	19	9	do	do	do	do	do	
959	80	−5	19	11	do	do	do	do	do	
960	76	+5	19	13	do	do	do	do	do	
961	70	−7	19	15	do	do	do	do	do	
962	80	+3	19	17	do	do	do	do	do	
963	70	−1	19	20	do	do	do	do	do	
964	70	0	19	21	do	do	do	do	do	
965	82	−7	19	24	do	do	do	do	do	
966	74	+1	19	26	do	do	do	do	do	
970	80	+6	19	28	do	do	do	do	do	
971	73	−1	19	30	do	do	do	do	do	
972	80	+3	19	32	do	do	do	do	do	

All of the rats lived to be sacrificed. None showed liver or kidney necrosis.

TABLE 9.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[30 c. c. 1/100 arsenic equivalent solution or 75 mg. arsphenamine per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						*Per ct.*	
158	125	+18	19	3	None	2 days	Killed	No definite change	No definite change	69	Few small liver abscesses; a few of the liver cells contain small fat droplets (fat stain, osmic acid).
130	198	− 2	23	4	Slight	do	do	Hyaline casts	Fat, trace		
170	170	+ 2	18	4	do	do	do	do	No definite change	76	Lung abscesses; few small liver abscesses; a few of the liver cells contain small and medium-sized fat droplets (fat stain, osmic acid).
138	160	+ 4	23	8	None	do	do	do	Fat, trace		
160	92	+11	19	10	do	do	do	No definite change	No definite change	78	A few of the liver cells contain a very few small fat droplets (fat stain, osmic acid).
139	170	+ 1	23	13	do	do	do	Hyaline casts	Fat, trace		
172	96	+ 6	18	13	Slight	do	do	No definite change	No definite change	67	
161	90	+ 7	19	15	None	do	do	do	do	77	
173	90	+ 4	18	18	Slight	do	do	do	do	80	
162	112	+ 7	19	20	None	do	do	Slight necrosis	do	81	
174	78	+13	19	23	Slight	do	do	No definite change	do	78	
163	88	+21	19	24	None	do	do	Slight necrosis	do	78	
175	82	+12	19	28	Slight	do	do	No definite change	do	78	

All of the rats lived to be sacrificed; 16 per cent showed very slight kidney necrosis.

TABLE 10.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[35 c. c. 1/100 arsenic equivalent solution or 87 mg. arsphenamine per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						*Per ct.*	
164	100	+10	17	5	Slight	2 days	Killed	Slight necrosis	Necrosis 1/6	87	
126	136	− 1	22	6	None	do	do	Casts	No definite change	....	
131	137	− 1	22	11	do	do	do	do	Fat, trace	....	A few of the liver cells contain small and medium-sized fat droplets (fat stain, osmic acid).
166	80	+ 7	18	14	Slight	do	do	No definite change	No definite change	83	Lungs contain petechiae.
134	148	− 2	22	17	None	do	do	do	Fat, trace	....	
167	82	+ 7	18	19	Slight	do	do	do	No definite change	83	
137	140	− 1	22	24	None	do	do	Slight necrosis	Fat, trace	....	
168	82	+ 1	18	24	Slight	do	do	No definite change	No definite change	89	
169	84	− 5	18	30	do	do	do	do	do	81	

All of the rats lived to be sacrificed; 22 per cent showed very slight kidney necrosis; 11 per cent showed slight liver necrosis.

TABLE 11.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[40 c. c. 1/100 arsenic equivalent solution or 99 mg. arsphenamine per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						*Per ct.*	
272	95	+ 3	19	5	Slight	2 days	Killed	No definite change	No definite change	68	Many small liver abscesses.
124	128	+ 1	19	6	do	do	do	do	do		Lung abscesses.
273	136	+ 7	19	9	do	do	do	Moderate necrosis; casts.	do	73	
274	76	+12	19	12	do	do	do	No definite change	do	84	
127	136	− 1	19	13	None	do	do	Casts	do		
276	82	+11	20	15	Slight	do	do	No definite change	do	76	
128	124	− 1	19	20	None	do	do	do	do		
275	72	+19	20	21	Slight	do	do	do	do	75	
290	156	− 3	19	22	do	do	do	Moderate necrosis	do	91	
277	87	+15	20	25	do	do	do	No definite change	do	79	
292	149	− 3	19	26	do	do	do	do	do	85	Lung abscesses.
278	82	+12	20	29	do	do	do	do	do	84	
296	151	+ 5	19	30	do	do	do	do	do	82	
136	134	+ 1	20	30	None	do	do	do	do		
571	86	+12	20	29	Slight	do	do	Slight necrosis	do		

All of the rats lived to be sacrificed; 20 per cent showed kidney necrosis.

TABLE 12.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[50 c. c. 1/100 arsenic equivalent solution or 124 mg. arsphenamine per kilo body weight.]

[Room temperature 24° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						*Per ct.*	
125	83	+ 4	18	4	Severe	22 hours	Died	Congestion; hemorrhages.	No definite change		Acute splenic tumor.
279	83	+16	18	4	Slight	2 days	Killed	Slight necrosis	do	82	Adrenals hemorrhagic.
285	96	+ 8	18	5	do	do	do	No definite change	do	83	
129	120	+ 2	18	9	do	do	do	Slight necrosis	Fat + +		Many of the liver cells contain small and medium sized fat droplets (fat stain, osmic acid).
280	74	+ 5	18	9	do	do	do	No definite change	No definite change	84	
286	94	+ 6	19	10	do	do	do	do	do	86	
281	76	+ 8	18	13	do	do	do	do	do	92	
132	110	− 2	19	14	do	do	do	do	do		
287	85	+ 6	19	15	do	do	do	do	do	81	
282	83	+13	18	18	Convulsions.	30 minutes	Died	Congestion; hemorrhages.	Congestion		Lungs and intestinal mucosa congested.
288	90	+ 4	19	19	Slight	2 days	Killed	No definite change	No definite change	86	
133	100	− 4	19	21	None	do	do	Casts	Congestion		
283	106	+ 9	18	26	Slight	do	do	No definite change	No definite change	86	
284	88	+ 9	18	31	do	do	do	do	do	91	
561	88	+14	19	19	Severe	21 minutes	Died	Congestion	Congestion		Acute lung picture; intestinal mucosa congested.
562	93	+11	19	24	do	3½ hours	do	do	do		Do.
563	89	+12	19	28	do	1½ hours	do	do	do		Do.
564	104	+ 3	19	31	do	8½ hours	do	Congestion; casts	do		Do.
565	129	+ 4	19	35	do	5 minutes	do	Congestion	do		Do.

Sixty-eight per cent of the rats lived over 12 hours; 16 per cent of these showed kidney necrosis. In some instances the adrenals were hemorrhagic. The rats that died acutely showed distention, congestion, edema, and petechiae of the lungs, and congestion of the abdominal viscera. Sixty-three per cent of the animals lived to be sacrificed.

TABLE 13.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[55 c. c. arsenic equivalent solution or 137 mg. arsphenamine per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
476	122	+11	19	16	Severe....	2¼ hours...	Died......	Congestion........	Congestion........	Pleural fluid increased; acute lung picture; intestinal mucosa and spleen congested.
477	120	+ 8	19	21	...do.......	8¼ hours...	...do.......	Congestion; hemorrhages.	.....do.............	Acute lung picture; intestinal mucosa congested.
478	114	+ 9	19	25	...do.......	1½ hours...	...do.......	Congestion........	.....do.............	Do.
479	93	+13	19	29	...do.......	2 days.....	Killed.....	Moderate necrosis; casts	No definite change.	
528	90	+10	19	18	Moderate..	...do........	...do.......	No definite change.	Many mitoses.....	
525	90	+ 9	19	23	Severe....	30 minutes	Died......	Congestion........	Congestion........	Pleural fluid increased; intestinal mucosa congested.
530	76	+16	19	27	...do.......	20 minutes	...do.......	.....do.............	.....do.............	Do.
532	90	+17	19	32	...do.......	3½ hours...	...do.......	.....do.............	.....do.............	Do.
480	112	+ 7	19	4	...do.......	1¼ hours...	...do.......	.....do.............	.....do.............	Do.
481	103	+ 5	19	8	...do.......	10 hours...	...do.......	Congestion; casts..	Congestion; hemorrhages.	Acute lung picture; intestinal mucosa congested.
482	102	+10	19	11	Moderate..	2 days.....	Killed.....	Slight necrosis; casts.	No definite change.	Lungs contain petechiae; adrenals hemorrhagic; many small liver abscesses.
483	102	+11	19	15	...do.......	...do.......	...do.......	.....do.............	.....do.............	Lungs contain petechiae; adrenals swollen and hemorrhagic.
484	110	+ 2	19	18	...do.......	...do.......	...do.......	Moderate necrosis; casts.	.....do.............	
485	95	+15	19	22	...do.......	...do.......	...do.......	Slight necrosis; casts.	.....do.............	Adrenals hemorrhagic.
533	93	+ 5	20	4	...do.......	3 hours....	Died......	Congestion........	Congestion........	Pleural fluid increased; intestinal mucosa and spleen congested.
534	94	+ 9	20	8	...do.......	1 hour.....	...do.......	.....do.............	.....do.............	Do.
535	96	+ 5	20	12	...do.......	9½ hours...	...do.......	Congestion; edema; hemorrhages; casts.	Congestion; hemorrhages.	Acute lung picture; adrenals hemorrhagic; thymus hemorrhagic.
536	86	+ 9	20	15	...do.......	2 days.....	Killed.....	Slight necrosis; casts.	No definite change	Lungs contain petechiae; adrenals hemorrhagic; many small liver abscesses.
537	87	+18	20	20	Severe....	1¾ hours...	Died......	Congestion........	Congestion........	Pleural fluid increased; acute lung picture; intestinal mucosa congested.
538	84	+14	20	23	Moderate..	2 days.....	Killed.....	Slight necrosis; casts.	Central necrosis ¼.	Lungs contain petechiae.

Forty per cent of the rats lived over 12 hours; 88 per cent of these showed kidney necrosis; 12 per cent showed central liver necrosis. The adrenals and thymus were hemorrhagic in a few instances. The rats that died acutely showed the usual lung picture and congestion of the intestinal mucosa. As a rule the pleural fluid was markedly increased. Forty per cent of the animals lived to be sacrificed.

TABLE 14.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[60 c. c 1/100 arsenic equivalent solution or 149 mg. arsphenamine per kilo body weight.]

[Room temperature 20-22° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
428	145	+ 8	....	6	Severe....	2 days.....	Killed.....	No definite change.	Fat+++.........	Lung abscesses and petechiae; many small liver abscesses.
432	150	+ 9	....	13	...do.......	6 hours....	Died......	Congestion........	Congestion; fat++	Acute lung picture; intestinal mucosa and spleen congested.
433	152	+ 7	....	18	...do.......	1 hour.....	...do.......	.....do............	Congestion........	Do.
435	148	+ 8	....	29	...do.......	45 minutes	...do.......	.....do............	.....do............	Do.
438	135	+11	....	9	...do.......	24¾ hours..	...do.......	Moderate necrosis; casts.	Necrosis ¼; fat++++.	Acute lung picture with abscesses; heart muscle contains petechiae; adrenals swollen and hemorrhagic; intestinal mucosa and spleen congested.
441	158	+ 6	....	15	...do.......	4 hours....	...do.......	Congestion; edema; hemorrhages.	Congestion; fat++	Acute lung picture; intestinal mucosa and spleen congested.
442	142	+ 7	....	20	...do.......	22 minutes	...do.......	Congestion........	Congestion........	Do.
443	142	+14	....	25	...do.......	13¾ hours..	...do.......	Slight necrosis; casts.	.....do............	Acute lung picture; intestinal mucosa and spleen congested; adrenals hemorrhagic.
444	146	+ 8	....	30	...do.......	2 days.....	Killed.....	Extensive necrosis; casts.	Fat++...........	Adrenals are swollen and hemorrhagic; many small liver abscesses.
456	112	+ 7	20	19	...do.......	8 minutes.	Died......	Congestion........	Congestion........	Acute lung picture; intestinal mucosa and spleen congested.
457	135	+ 2	20	22	...do.......	5 minutes.	...do.......	.....do............	.....do............	Do.
458	139	+ 7	20	27	...do.......	...do.......	...do.......	.....do............	.....do............	Do.
459	112	+10	20	30	...do.......	30 minutes	...do.......	.....do............	.....do............	Do.
460	108	+12	22	5	...do.......	11 minutes	...do.......	.....do............	.....do............	Do.
461	134	+ 9	22	10	...do.......	2½ hours...	...do.......	Congestion; hemorrhages.	Congestion; hemorrhages.	Do.
462	136	+ 2	22	15	...do.......	11 minutes	...do.......	Congestion........	Congestion; edema.	Do.
464	110	+ 4	22	26	...do.......	42¾ hours..	...do.......	Moderate necrosis.	Central necrosis ⅓ to ½; fat++.	
465	100	+ 3	22	31	...do.......	45 minutes	...do.......	Congestion........	Congestion........	Do.

Twenty-eight per cent of the rats lived over 12 hours; 80 per cent of these showed kidney necrosis; 40 per cent showed central liver necrosis. In a few cases the heart muscle contained petechiae and the adrenals were hemorrhagic. The acute deaths were characterized by distention, congestion, edema and petechiae of the lungs and congestion of the abdominal viscera. Eleven per cent of the rats lived to be sacrificed.

Table 15.—*Arsphenamine (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[70 c. c. 1/100 arsenic equivalent solution or 174 mg. arsphenamine per kilo body weight.]

[Room temperature 20–22° C.]

Rat.	Initial weight.	Weight loss or gain.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per cent.*	*Mins.*						
426	128	+ 9	12	Severe	9 minutes	Died	Congestion	Congestion	Acute lung picture; intestinal mucosa and spleen congested.
427	132	+ 9	21	do	35 minutes	do	do	do	Do.
429	98	+18	26	do	4 hours	do	do	do	Do.
430	112	+11	36	do	10 minutes	do	do	do	Acute lung picture; lung abscesses; intestinal mucosa and spleen congested.
431	138	+ 7	43	do	1½ hours	do	do	do	Acute lung picture; intestinal mucosa congested.
436	120	+ 8	4	do	4½ hours	do	Congestion; casts	Congestion; hemorrhages.	Acute lung picture; heart muscle contains petechiæ; adrenals hemorrhagic; intestinal mucosa and spleen congested.
437	120	+ 8	8	do	1¼ hours	do	Congestion	Congestion	Acute lung picture; intestinal mucosa congested.
439	122	+ 8	13	do	9 minutes	do	do	do	Do.
440	124	+11	21	do	30 minutes	do	do	do	Acute lung picture; lung abscesses; adrenals hemorrhagic; intestinal mucosa congested.
445	126	+ 9	28	do	2¼ hours	do	do	do	Acute lung picture; intestinal mucosa and spleen congested.

All of the rats died within 4½ hours and showed distention, congestion, edema, and petechiæ of the lungs. **As a rule the mucosa of the small intestine was markedly congested. In some cases the heart muscle contained petechiæ and the adrenals were hemorrhagic.**

TABLE 16.—*Arsphenamine (sodium salt)—Rats injected intravenously after a three-day fast.*

[10 c. c. 1/100 arsenic equivalent solution or 25 mg. arsphenamine per kilo body weight.]

[Room temperature 22–26° C.]

Rat.	Initial weight.	Weight loss during fast.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per cent.*	*Mins.*						*Per cent.*	
312	76	−13	3	Slight	2 days	Killed	No definite change	No definite change	110	
313	99	−13	6	do	do	do	do	do	111	
314	83	−16	8	do	do	do	do	do	115	
315	84	−23	11	do	46 hours	Died	Congestion; hemorrhages.	Congestion		Adrenals hemorrhagic.
316	101	−11	13	do	2 days	Killed	No definite change	No definite change	95	
317	117	−13	16	do	do	do	do	do	99	
311	84	−13	28	do	do	do	do	do	108	
370	113	− 4	3	None	do	do	do	do	89	
371	111	− 6	6	do	do	do	do	do	95	
372	96	− 6	8	do	do	do	do	do	90	
373	108	−10	10	do	do	do	do	do	105	
374	113	− 6	13	do	do	do	do	do	100	
375	116	−10	15	do	18 hours	Died	Congestion	Congestion		
366	112	− 5	22	do	2 days	Killed	No definite change	No definite change	86	Spleen congested.
367	121	− 9	24	do	do	do	do	do	103	
368	113	− 4	26	do	do	do	do	do	84	
369	106	− 9	29	do	do	do	do	do	104	

All of the rats lived 18 hours or longer; none showed kidney or liver necrosis; 88 per cent lived to be sacrificed.

TABLE 17.—*Arsphenamine (sodium salt)—Rats injected intravenously after a three-day fast.*

[20 c. c. 1/100 arsenic equivalent solution or 50 mg. arsphenamine per kilo body weight.]

[Room temperature 23–26° C.]

Rat.	Initial weight.	Weight loss during fast.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Mins.*						*Per ct.*	
304	83	−14	4	Slight	2 days	Killed	No definite change	No definite change	102	
305	116	−13	8	do	do	do	do	do	96	
306	87	−17	11	do	47 hours	Died	do	Congestion		
307	90	−14	15	do	2 days	Killed	do	No definite change	104	
308	81	−16	18	do	do	do	do	do	99	
309	74	−19	21	do	44 hours	Died	do	do		Diarrhea.
310	123	−11	24	do	2 days	Killed	do	do	102	
362	145	−10	3	None	do	do	do	do	87	
363	132	−14	7	do	do	do	do	do	85	
356	112	−14	12	do	do	do	do	do	96	
357	138	−14	14	do	do	do	Slight necrosis	do	96	
364	130	−11	16	do	do	do	No definite change	do	87	
358	144	−12	17	do	do	do	Slight necrosis	Fat, trace	103	
365	132	−12	19	do	do	do	No definite change	No definite change	96	
359	125	−17	22	do	do	do	do	do	111	
360	114	−12	26	do	do	do	do	do	81	
361	136	−18	30	do	do	do	do	do	96	
420	100	−21	2	do	do	do	do	do	112	Adrenals congested.
421	100	−18	4	do	do	do	do	do	98	
422	104	−17	6	do	do	do	do	do	96	
423	122	−14	8	do	do	do	do	do	100	
424	120	−18	11	do	do	do	do	do	107	
425	96	−16	14	do	do	do	do	do	102	

All of the rats lived 44 hours or longer; 0.9 per cent showed kidney necrosis; 91 per cent lived to be sacrificed.

TABLE 18.—*Arsphenamine (sodium salt)—Rats injected intravenously after a three-day fast.*

[30 c. c. 1/100 arsenic equivalent solution or 75 mg. arsphenamine per kilo body weight.]

[Room temperature 23–26° C.]

Rat.	Initial weight.	Weight loss during fast.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Mins.*						*Per ct.*	
404	106	−13	3	Slight	2 days	Killed	No definite change	No definite change	84	
405	98	−12	5	Severe	7 minutes	Died	Congestion	Congestion		Lungs congested and contain petechiae.
406	124	−14	9	Slight	2 days	Killed	No definite change	No definite change	85	
407	88	−19	11	do	do	do	do	do	95	
414	133	−18	15	do	do	do	do	do	97	
415	130	−17	18	do	do	do	Slight necrosis	do	104	
416	116	−21	21	Severe	14 minutes	Died	Congestion; hemorrhages.	Congestion		Lungs congested and contain petechiae; lung abscesses.
417	130	−15	24	Slight	2 days	Killed	Slight necrosis	No definite change	91	
418	116	−13	26	do	do	do	do	Fat + + +	81	Many small and medium sized fat droplets mainly in central 2/3 of liver lobules (fat stain, osmic acid).
419	124	−13	29	do	do	do	do	No definite change	106	

Eighty per cent of the rats lived to be sacrificed; 50 per cent of these showed kidney necrosis.

TABLE 19.—*Arsphenamine (sodium salt)—Rats injected intravenously after a three-day fast.*

[40 c. c. 1/100 arsenic equivalent solution or 99 mg. arsphenamine per kilo body weight.]

[Room temperature 23–26° C.]

Rat.	Initial weight.	Weight loss during fast.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*	*Mins.*						*Per ct.*	
343	104	−12	3	None	2 days	Killed	Moderate necrosis.	Central necrosis ½	87	
336	135	− 5	4	do	32 hours	Died	Extensive necrosis	Central necrosis ⅓ to ⅗; fat++		
344	124	−10	6	do	2 days	Killed	No definite change	Fat+++	83	Many small and medium sized fat droplets mainly in central ⅔ of liver lobules (fat stain, osmic acid).
345	112	− 9	9	do	do	do	Casts; fat+++	Fat+++	78	Many small and medium sized fat droplets in liver cells; also in parenchyma cells of convoluted tubules and medullary striae of the kidney (fat stain, osmic acid).
337	118	−10	9	do	do	do	Moderate necrosis.	Central necrosis ½	95	
339	145	−10	17	do	do	do	Slight necrosis	Central necrosis ⅓ to ⅗.	100	Lungs contain petechiae.
340	120	−13	22	do	do	do	Moderate necrosis.	No definite change.	100	Lung abscesses.
341	133	−11	26	do	do	do	do	do	93	
342	122	− 9	30	do	do	do	Slight necrosis	Fat++	71	Many of the liver cells contain small and medium sized fat droplets (fat stain, osmic acid).
388	105	−15	4	Severe	do	do	Extensive necrosis	Central necrosis ⅓	76	Adrenals hemorrhagic.
378	120	−16	5	do	8 minutes	Died	Congestion	Congestion		Lungs congested, oedematous and contain petechiae.
384	94	−18	6	do	4½ hours	do	do	do		
389	110	−13	8	do	10 minutes	do	do	do		Lungs congested.
379	105	−17	10	do	5 minutes	do	do	do		Do.
390	178	−13	12	do	8 minutes	do	do	do		Do.
385	130	−16	12	do	2 days	Killed	Moderate necrosis.	Fat, trace (osmic acid).	81	Lungs contain petechiae.
380	105	−16	15	do	5 minutes	Died	Congestion	Congestion		
391	117	−10	16	do	2 days	Killed	No definite change.	No definite change.	74	
381	122	−17	20	do	do	do	Moderate necrosis.	do	84	Do.
387	134	−15	21	do	10 hours	Died	Congestion	do		
392	138	−14	22	do	8 minutes	do	do	Congestion		Lungs congested.
382	96	−17	24	do	7 hours	do	do	Fat, trace (osmic acid).		
393	188	−11	25	do	2 days	Killed	Extensive necrosis.	Central necrosis ⅓ to ⅗.	92	
383	138	−13	30	do	29 hours	Died	Interstitial hemorrhages.	Congestion		Lungs congested and contain abscesses.

Sixth-three per cent of the rats lived 12 hours or longer; 73 per cent of these showed kidney necrosis; 40 per cent showed central liver necrosis. Only a few of the animals that died acutely showed congestion, edema and petechiae of lungs. Fifty-four per cent of the rats lived to be sacrificed.

TABLE 20.—*Arsphenamine (sodium salt)—Rats injected intravenously after a three-day fast.*

[50 c. c. 1/100 arsenic equivalent solution or 124 mg. arsphenamine per kilo body weight.]

[Room temperature 23-26° C.]

Rat.	Initial weight.	Weight loss during fast.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Mins.*						
396	134	−16	5	Severe	2 days	Killed	Moderate necrosis.	Central necrosis 4/5	Adrenals hemorrhagic.
397	98	−16	9	do.	6 minutes.	Died	Congestion	Congestion	Lungs congested.
398	82	−14	12	do.	3 minutes.	do.	do.	do.	Do.
399	103	−15	16	do.	10 minutes	do.	do.	do.	Do.
400	120	−15	23	do.	12 hours	do.	Slight necrosis	do.	Lungs congested and edematous.
401	119	−14	27	do.	6 hours	do.	Congestion; hemorrhage.	do.	Do.
402	86	−16	29	do.	8 hours	do.	do.	do.	
394	120	−16	29	do.	46 minutes	do.	do.	do.	Do.
403	88	−20	32	do.	8 minutes.	do.	do.	do.	Do.
395	163	− 9	35	do.	25 hours	do.	Moderate necrosis.	Central necrosis 1/3 to 4/5.	Lungs edematous and contain petechiae; adrenals hemorrhagic.

Thirty per cent of the rats lived 12 hours or longer; 100 per cent of these showed kidney necrosis; 67 per cent showed central liver necrosis. In some instances the adrenals were hemorrhagic. The animals that died acutely showed congestion, edema, and petechiae of the lungs. Ten per cent of the animals lived to be sacrificed.

TABLE 21.—*Control rats sacrificed after a five-day fast.*

Rat.	Initial weight.	Weight loss during fast.	Length of life.	Termination.	Kidney.	Liver.	Hemoglobin at death (heart blood).	Remarks.
	Gm.	*Per ct.*					*Per ct.*	
408	114	−16	5 days	Killed	No change	No change	107	
409	102	−13	do.	do.	do.	do.	94	
410	130	−13	do.	do.	do.	do.	66	
411	135	−13	do.	do.	do.	do.	87	
412	109	−14	do.	do.	do.	do.	111	
413	90	−16	do.	do.	do.	do.	95	Few small liver abscesses.

TABLE 22.—*Arsphenamine (sodium salt)—Rats injected intravenously after three days on 40 per cent saccharose solution.*[1]

[20 c. c. 1/100 arsenic equivalent solution or 50 mg. arsphenamine per kilo body weight.]

[Room temperature 19-25° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
609	96	− 6		36	Severe	9 minutes	Died	Congestion	Congestion	Acute lung picture.
610	103	− 8		39	do	3¼ hours	do	do	do	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
611	99	− 7		41	Moderate	2 days	Killed	No definite change	No definite change	
612	93	− 6		44	Severe	11 hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
613	89	− 5		3	Moderate	2 days	Killed	Slight necrosis	No definite change	Tapeworm cyst in liver.
614	92	− 7		6	Severe	4½ hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
615	88	− 3		9	Moderate	2 days	Killed	Casts	No definite change	
616	100	− 6		12	do	do	do	do	do	
617	102	− 9		16	Severe	15 hours	Died	No definite change	do	Lungs distended and somewhat edematous.
618	95	− 8		18	do	2¼ hours	do	Congestion	Congestion	Acute lung picture.
619	96	− 8		23	do	do	do	do	do	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
620	96	− 2		25	Moderate	2 days	Killed	No definite change	No definite change	
621	113	− 8	18	8	do	do	do	do	do	Hemoglobin 58 per cent.
622	108	−11	18	11	do	do	do	do	do	Hemoglobin 67 per cent.
623	109	−13	18	14	do	do	do	do	do	Hemoglobin 71 per cent; tapeworm cysts in liver.
624	147	− 8	18	17	do	do	do	do	do	Hemoglobin 73 per cent.
625	105	−16	18	21	do	do	do	do	do	Hemoglobin 45 per cent.; adrenals hemorrhagic; many small liver abscesses.
626	117	− 9	18	25	do	do	do	Slight necrosis; casts.	do	Hemoglobin 74 per cent.
627	109	−11	18	29	do	do	do	Congestion	do	
628	109	− 9	18	32	do	do	do	Slight necrosis	do	
637	160	−11	23	9	do	do	do	No definite change	do	
638	140	− 8	23	13	do	20 hours	Died	Congestion; hemorrhages.	Congestion	Lungs congested.
639	144	− 9	23	16	do	7 hours	do	Congestion	do	Acute lung picture; tapeworm cysts in liver.
640	132	−10	23	19	do	2 days	Killed	Moderate necrosis	No definite change	
641	112	−11	23	22	do	do	do	No definite change	do	
642	135	− 7	23	26	do	do	do	do	do	
643	152	−12	23	30	do	do	do	do	do	Tapeworm cysts in liver.
644	142	−11	23	33	do	do	do	do	do	

[1] Rats consumed from 12 to 15 c. c. daily

Seventy-five per cent of the rats lived 12 hours or longer; 19 per cent of these showed kidney necrosis. All of the rats that died acutely showed distention, congestion, edema, and petechiae of lungs. In some of the animals the pleural fluid was markedly increased. As a rule the abdominal viscera were congested. Sixty-eight per cent of the animals lived to be sacrificed.

TABLE 23.—*Arsphenamine (sodium salt)—Rats injected intravenously after three days on 40 per cent saccharose solution.*[1]

[30 c. c. 1/100 arsenic equivalent solution or 75 mg. arsphenamine per kilo body weight.]

[Room temperature 19–25° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
646	124	−10	18	9	Moderate	2 days	Killed	Slight necrosis	No definite change.	
647	145	−12	18	13	do	do	do	Moderate necrosis.	do	
648	137	− 8	18	17	do	do	do	Slight necrosis; casts.	do	Many small liver abscesses.
649	119	−11	18	21	do	do	do	Slight necrosis	do	Liver contains a tapeworm cyst.
650	140	−16	18	26	do	do	do	No definite change.	do	
651	112	−11	18	30	do	do	do	Slight necrosis	do	
652	125	− 8	18	34	do	do	do	do	do	
653	143	−10	18	38	do	36 hours	Died	do	do	Diarrhea; lung abscesses; many small liver abscesses.
660	118	−10	23	12	do	8½ hours	do	Congestion	Congestion	Acute lung picture; lung abscesses.
661	142	−11	23	16	do	2 days	Killed	Moderate necrosis.	No definite change.	
662	117	−11	23	21	do	47½ hours	Died	Slight necrosis	do	
663	137	− 9	23	25	do	2 days	Killed	Moderate necrosis; casts.	do	
664	154	−11	23	31	do	do	do	do	do	
665	127	−11	23	35	do	47½ hours	Died	Moderate necrosis.	Congestion	
666	121	− 7	23	39	do	6 hours	do	Slight congestion.	Slight congestion.	Acute lung picture; liver contains tapeworm cysts.
597	83	0		20	Severe	45 minutes.	do	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
598	86	− 2		25	do	3¼ hours	do	do	do	Do.
599	97	− 2		29	Moderate	2 days	Killed	Moderate necrosis; casts.	No definite change.	Adrenals hemorrhagic.
600	94	0		5	Severe	4 hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
601	104	− 4		9	do	1½ hours	do	do	do	Do.
602	90	− 4		12	do	40 minutes.	do	do	do	Do.
603	92	− 1		15	do	1 hour	do	do	do	Do.
604	98	− 3		18	do	30 minutes.	do	do	do	Do.
605	86	+ 1		21	do	25 minutes.	do	do	do	Do.
606	100	− 2		25	do	1¾ hours	do	do	do	Do.
607	102	− 7		29	do	1 hour	do	do	do	Do.
608	104	− 8		33	do	1½ hours	do	do	do	Do.

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[1] Rats consumed 12 to 15 c. c. daily.

Fifty-two per cent of the rats lived 12 hours or longer; 93 per cent of these showed kidney necrosis. All of the rats that died acutely showed distention, congestion, edema and petechiæ of lungs, and congestion of abdominal viscera. As a rule the pleural fluid was markedly increased. Forty-one per cent of the animals lived to be sacrificed.

TABLE 24.—*Arsphenamine (sodium salt)—Rats injected intravenously after three days on 40 per cent saccharose solution.*[1]

[40 c. c. 1/100 arsenic equivalent solution or 99 mg. arsphenamine per kilo body weight.]

[Room temperature, 23–25° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
671	158	− 9	22	12	Severe	2 days	Killed	Slight necrosis; casts.	No definite change	Diarrhea; lung abscesses; liver contains tapeworm cysts and many small abscesses.
672	143	− 5	22	16	do	14 minutes	Died	Congestion	Congestion	Acute lung picture; intestinal mucosa congested.
673	127	− 6	22	20	do	2 days	Killed	Extensive necrosis; casts.	No definite change	
674	127	− 4	22	25	do	53 minutes	Died	Congestion	Congestion	Do.
675	130	− 6	22	30	do	1 hour	do	do	do	Acute lung picture; lung abscesses; intestinal mucosa congested.
676	160	− 8	22	38	do	25 minutes	do	do	do	Do.
677	128	− 9	22	44	do	21 hour	do	Slight necrosis	do	Lung abscesses; adrenals hemorrhagic.
678	108	− 6	23	5	do	11½ hours	do	Congestion	do	Adrenals hemorrhagic; liver contained tapeworm cyst.
679	154	− 6	23	10	do	5 minutes	do	do	do	Acute lung picture; intestinal mucosa congested.
680	128	−12	23	15	do	2 days	Killed	Moderate necrosis; casts.	No definite change	Lungs contain a few petechiae; many small liver abscesses.
681	146	− 3	23	20	do	6½ hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased.
682	136	− 6	23	24	do	20 hours	do	Congestion; hemorrhages.	Marked congestion	
683	132	−12	23	30	do	13¼ hours	do	do	Congestion	Lung abcesses; liver contains a tapeworm cyst.
684	148	− 8	23	35	do	2 days	Killed	Moderate necrosis; casts.	No definite change	Diarrhea. Lung abscesses.
685	147	− 5	23	39	do	36 minutes	Died	Congestion	Congestion	Acute lung picture; intestinal mucosa congested.
686	127	− 6	22	7	do	18 minutes	do	do	do	Do.
696	133	−11	18	9	Moderate	2 days	Killed	Extensive necrosis; casts.	No definite change	Liver contains a tapeworm cyst.
697	114	− 9	18	14	do	do	do	do	do	
698	134	−10	18	17	do	do	do	do	do	
699	133	−10	18	21	do	do	do	do	do	Adrenals hemorrhagic.
700	126	−11	18	24	do	do	do	do	Central necrosis ¼	Adrenals swollen.
701	144	−10	18	29	do	do	do	Slight necrosis	No definite change	
702	122	−18	18	33	Severe	27 minutes	Died	Congestion	Congestion	Acute lung picture.
703	148	− 9	18	41	Moderate	2 days	Killed	Extensive necrosis; casts.	No definite change	Many small liver abscesses.
704	134	− 7	19	9	Severe	6 minutes	Died	Congestion	Congestion	Acute lung picture.
705	135	− 9	19	14	do	2¼ hours	do	do	do	Acute lung picture; lung abscesses; acute splenic tumor.
706	131	− 7	19	21	Moderate	2 days	Killed	Extensive necrosis.	No definite change	

707	151	−10	19	25	...do......	...do......	...do......	Moderate necrosis.	.....do.............	
708	90	−14	19	38	Severe....	6 hours....	Died......	No definite change.	.....do.............	Diarrhea; acute lung picture.
709	98	−14	19	32	Moderate .	2 days.....	Killed.....	.....do.............	.....do.............	
710	115	−10	19	37	Severe....	22 hours...	Died......	Congestion........	.....do.............	Acute lung picture.
585	92	− 1	....	16	...do......	1½ hours...	...do......	.....do.............	Congestion........	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
586	88	− 2	....	21	...do......	1¼ hours...	...do......	.....do.............	.....do.............	Do.
587	90	− 2	....	24	...do......	3 hours....	...do......	.....do.............	.....do.............	Do.
588	87	− 3	....	29	Moderate .	2 days.....	Killed.....	No definite change.	No definite change	
589	86	− 7	....	32	...do......	...do......	...do......	.....do.............	....do.............	
590	89	− 2	....	35	Severe....	2¾ hours...	Died......	Congestion........	Congestion........	Acute lung picture; pleural fluid increased; intestinal mucosa congested; adrenals hemorrhagic.
591	90	− 1	....	38	...do......	1¾ hours...	...do......	.....do.............	.....do.............	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
592	100	− 7	....	42	...do......	1¼ hours...	...do......	.....do.............	.....do.............	Do.
593	86	− 2	....	4	...do......	4¾ hours...	...do......	.....do.............	.....do.............	Do.
594	89	− 2	....	7	...do......	2¼ hours...	...do......	Congestion; hemorrhages; casts.	.....do.............	Do.
595	86	− 1	....	12	...do......	20 minutes	...do......	Congestion........	.....do.............	Do.
596	82	+ 1	....	17	...do......	2¼ hours...	...do......	Congestion; hemorrhages.	.....do.............	Do.

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[1] Rats consumed from 12 to 15 c. c. daily.

Forty-six per cent of the rats lived 12 hours or longer; 70 per cent of these showed kidney necrosis; 5 per cent showed central liver necrosis. The adrenals were hemorrhagic in some cases. All of the animals that died acutely showed distention, congestion, edema, and petechiae of the lungs and congestion of the abdominal viscera. As a rule the pleural fluid was markedly increased. Thirty-seven per cent lived to be sacrificed.

Table 25.—*Arsphenamine (sodium salt)—Rats injected intravenously after three days on 40 per cent saccharose solution.*[1]

[50 c. c. 1/100 arsenic equivalent solution or 124 mg. arsphenamine per kilo body weight.]

[Room temperature, 24-25° C.]

Rat.	Initial weight.	Weight loss or gain.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Mins.*						
572	85	−2	6	Severe	4 hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
573	87	0	11	Moderate	2 days	Killed	Slight necrosis	No definite change	
574	87	−1	15	Severe	3½ hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested; thymus hemorrhagic.
575	88	−2	19	do	2½ hours	do	do	do	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
576	94	−1	23	do	2 hours	do	do	do	Acute lung picture; pleural fluid increased; intestinal mucosa congested; adrenals hemorrhagic.
577	91	0	27	Moderate	2 days	Killed	Moderate necrosis; casts.	No definite change	Do.
578	88	0	30	Severe	3¾ hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
579	90	0	33	do	6½ hours	do	do	do	Do.
580	95	0	36	Moderate	2 days	Killed	Slight necrosis; casts.	No definite change	
581	93	−1	42	Severe	2 hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested; adrenals hemorrhagic; diarrhea.
582	103	−3	4	do	5 hours	do	do	do	Acute lung picture; pleural fluid increased; intestinal mucosa congested.
583	93	−2	8	Moderate	2 days	Killed	Moderate necrosis; casts.	No definite change	
584	106	−1	12	Severe	3¼ hours	Died	Congestion	Congestion	Acute lung picture; pleural fluid increased; intestinal mucosa congested; adrenals, thymus hemorrhagic.

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[1] Rats consumed from 12 to 15 c. c. daily.

Thirty-one per cent of the rats lived; all of these showed kidney necrosis; in some cases the adrenals and thymus were hemorrhagic. The rats that died acutely showed distention, congestion, edema, and petechiae of the lungs. As a rule the pleural fluid was markedly increased.

TABLE 26.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[15 c.c. 1/100 arsenic equivalent solution or 59 mg. neoarsphenamine per kilo body weight.]

[Room temperature, 22° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
967	104	−2	19	2	Slight	5 days	Killed	No definite change.	No definite change.	Lung abscesses.
968	90	0	19	4	do	do	do	do	do	
969	85	−4	19	6	do	do	do	do	do	
973	72	+4	19	8	do	do	do	do	do	
974	90	+6	19	10	do	do	do	do	do	Do.
975	90	+7	19	12	do	do	do	do	do	
976	80	+5	19	14	do	do	do	do	do	
977	80	+3	19	15	do	do	do	do	do	
978	88	+5	19	17	do	do	do	do	do	
979	83	+4	19	19	do	do	do	do	do	
980	90	−3	19	21	do	do	do	do	do	
981	86	−6	19	24	do	do	do	do	do	
982	140	−3	19	27	do	do	do	do	do	Pregnant.
983	80	+4	19	29	do	do	do	do	do	
984	72	−1	19	31	do	do	do	do	do	

All of the rats lived to be sacrificed; none showed kidney or liver necrosis.

TABLE 27.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[20 c.c. 1/100 arsenic equivalent solution or 79 mg. neoarsphenamine per kilo body weight.]

[Room temperature, 22–26° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
926	114	+7	22	4	Slight	5 days	Killed	Slight necrosis; casts.	No definite change.	
927	116	+6	22	6	do	do	do	do	Fat+	
928	110	−24	22	9	do	do	do	Casts	No definite change.	
929	98	+6	22	2	do	do	do	No definite change.	do	
937	186	+2	22	11	do	do	do	Moderate necrosis; casts.	do	Many small liver abscesses.
938	150	−6	22	14	do	do	do	No definite change.	do	
939	104	+9	22	23	do	do	do	do	do	
940	148	−4	22	25	do	do	do	do	do	
941	154	+5	22	5	do	do	do	do	do	Lung abscesses.
942	185	+5	22	27	do	do	do	Moderate necrosis; casts.	do	Lungs contain abscesses and a few petechiæ; many small liver abscesses.
943	112	+3	22	6	do	do	do	No definite change.	do	Lungs contain abscesses; many small liver abscesses.
944	144	+1	22	10	do	do	do	do	do	Many small liver abscesses.
945	144	+1	22	12	do	do	do	do	do	Lung abscesses and many small liver abscesses.
946	146	+4	22	15	do	do	do	Casts	do	Lung abscesses.
948	95	0	22	18	do	do	do	No definite change.	do	Liver contains a tapeworm cyst; extensive lung abscesses.

All of the rats lived to be sacrificed; 27 per cent showed kidney necrosis.

TABLE 28.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats and milk.*

[30 c. c. 1/100 arsenic equivalent solution or 118 mg. neoarsphenamine per kilo body weight.]

[Room temperature 19.5–21° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
750	85	−13	19	12	Severe	1¼ hours	Died	Congestion	No definite change.	Lung abscesses; many small liver abscesses.
751	93	+ 3	19	20	Slight	5 days	Killed	No definite change.	do	
752	108	− 9	19	27	do	do	do	do	do	Many lung abscesses and several small liver abscesses.
753	132	+ 3	19	37	do	do	do	Interstitial hemorrhage; casts.	do	
754	94	+ 6	19	44	do	do	do	No definite change.	do	Many small liver abscesses.
755	102	+11	22	5	do	do	do	Moderate necrosis; casts.	do	
756	132	+ 2	22	15	do	do	do	Slight necrosis; casts.	No mitoses; fat + +.	
757	102	+ 6	22	20	do	do	do	No definite change.	No definite change.	
758	98	+ 5	22	27	do	do	do	Slight necrosis; casts.	do	
759	83	+ 8	22	31	do	do	do	No definite change.	do	Coccidiosis.
760	100	+ 6	22	3	do	do	do	Few casts	do	
761	92	− 2	22	9	do	do	do	No definite change.	do	Lung abscesses.
762	83	+ 4	22	15	do	do	do	do	do	
763	100	+ 3	22	21	do	do	do	do	do	Do.
764	98	0	22	26	do	do	do	do	do	Do.

Ninety-three per cent of the rats lived to be sacrificed; 21 per cent of these showed kidney necrosis.

TABLE 29.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats and milk.*

[40 c. c. 1/100 arsenic equivalent solution or 157 mg. neoarsphenamine per kilo body weight.]

[Room temperature 18-19° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
765	84	+ 7	19	5	Slight	5 days	Killed	Moderate necrosis; casts.	No definite change.	Lung abscesses.
766	93	+ 4	19	10	...do	...do	...do	Slight necrosis; casts.	...do	
767	80	− 2	19	15	...do	...do	...do	No definite change.	...do	
768	68	+ 6	19	24	...do	...do	...do	Slight necrosis	...do	
769	67	0	19	30	Moderate	9¼ hours	Died	Congestion	...do	
770	70	+ 8	19	3	Slight	5 days	Killed	Slight necrosis; casts.	...do	Miliary abscesses in spleen and liver.
771	75	+ 7	19	7	...do	...do	...do	No definite change.	...do	
773	92	+ 7	19	13	...do	...do	...do	Extensive necrosis; casts.	...do	Lung abscesses.
774	82	−10	19	20	...do	...do	...do	No definite change.	...do	
775	166	+ 4	22	7	...do	...do	...do	Extensive necrosis; casts.	...do	
776	74	+ 7	22	14	...do	...do	...do	Slight necrosis; casts.	...do	Miliary abscesses in spleen and liver.
777	75	+ 1	22	20	...do	...do	...do	No definite change.	...do	Miliary abscesses in spleen.
779	63	+11	22	30	...do	...do	...do	Slight necrosis	...do	Do.

Ninety-two per cent of the rats lived to be sacrificed; 67 per cent of these showed kidney necrosis.

TABLE 30.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[50 c. c. 1/100 arsenic solution or 197 mg. neoarsphenamine per kilo body weight.]

[Room temperature 22-24° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
780	86	+ 9	19	6	Slight	5 days	Killed	Slight necrosis	No definite change	Lung abscesses.
781	116	+ 7	19	14	do	do	do	Moderate necrosis	do	Do.
782	104	+10	19	25	do	do	do	Moderate necrosis; casts.	do	
783	66	+ 6	19	33	do	do	do	No definite change.	do	Many lung abscesses.
784	136	+ 4	20	5	do	do	do	Extensive necrosis; casts.	do	
785	74	+ 4	20	10	do	do	do	Moderate necrosis; casts.	do	
786	81	+ 4	20	15	do	do	do	do	do	
787	70	− 4	20	20	do	do	do	Extensive necrosis; casts.	No mitoses	
788	72	− 1	20	25	do	do	do	do	No definite change	Lung abscesses.
789	54	+ 6	20	30	do	do	do	Slight necrosis; casts.	do	
790	90	+ 8	21	6	do	do	do	Extensive necrosis; casts.	do	
791	76	+ 8	21	12	do	do	do	do	do	Lungs distended and contain abscesses.
792	52	+19	21	20	do	do	do	Slight necrosis	do	
793	63	+16	21	25	do	do	do	Moderate necrosis; casts.	do	
794	56	+19	21	30	Severe	45 minutes	Died	Cells swollen, very granular, especially in boundary zone of medulla.	Congestion	Many small liver abscesses.

Ninety-three per cent of the rats lived to be sacrificed; 87 per cent of these showed kidney necrosis.

TABLE 31.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[60 c. c. 1/100 arsenic equivalent solution or 236 mg. neoarsphenamine per kilo body weight.]

[Room temperature 16° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
805	100	+ 6	23	40	Slight	5 days	Killed	Extensive necrosis; casts.	No definite change	
806	89	+ 3	23	46	do	do	do	do	do	
807	100	+ 8	23	5	do	do	do	do	do	
808	86	+ 9	23	10	do	do	do	do	do	
809	71	+ 4	23	14	do	do	do	Slight necrosis	do	Lung abscesses.
810	82	+11	23	19	do	do	do	Extensive necrosis; casts.	do	
811	86	+10	23	24	do	do	do	Slight necrosis	do	
812	67	+ 6	23	28	do	do	do	Moderate necrosis	do	
813	93	+ 9	23	33	do	do	do	Slight necrosis	do	
814	73	+ 1	23	38	do	do	do	Extensive necrosis; casts.	do	
820	88	+ 8	23	9	do	do	do	do	do	
821	74	+ 3	23	16	do	do	do	Slight necrosis; casts.	do	
822	70	+ 9	23	21	do	do	do	do	do	
823	80	+ 5	23	26	do	3 hours	Died	Cloudy swelling; edema.	do	Organs exsanguinated.
824	93	+ 5	23	34	do	5 days	Killed	Very extensive necrosis; casts.	do	

Ninety-three per cent of the rats lived to be sacrificed; all of these showed kidney necrosis.

TABLE 32.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[70 c. c. 1/100 arsenic equivalent solution, or 275 mg. neoarsphenamine per kilo body weight.]

[Room temperature 16° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkalin solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
795	70	+14	19	5	Severe	21½ hours.	Died	Cloudy swelling	No definite change.	Bled profusely; organs exsanguinated; lungs edematous.
796	86	+ 9	19	11	Slight	5 days	Killed	Moderate necrosis.	do	Bled profusely.
797	91	+14	19	18	do	do	do	Slight necrosis	do	Bled profusely; lung abscesses.
798	78	+13	19	23	do	do	do	No definite change.	do	Bled profusely.
799	82	+12	19	29	do	do	do	Extensive necrosis; casts.	do	Do.
800	82	+ 1	19	34	do	do	do	Moderate necrosis.	do	
801	86	+ 8	19	42	do	do	do	do	do	Do.
802	88	+ 5	21	5	do	4 days	Died	Extreme necrosis; calcification.	No mitoses	Do.
803	68	+13	21	14	do	5 days	Killed	Moderate necrosis.	No definite change.	
804	70	+ 6	21	20	do	do	do	Extensive necrosis; calcification; casts.	do	Do.
815	60	+12	21	35	do	do	do	Moderate necrosis; casts.	do	
816	63	+21	21	39	do	do	do	Extensive necrosis; casts.	do	
817	60	+ 7	21	43	do	do	do	do	do	
818	73	+10	21	47	do	do	do	do	do	
819	84	+10	21	4	do	do	do	Moderate necrosis; casts.	do	
835	95	+ 9	21	8	do	do	do	Very extensive necrosis; casts.	do	
836	115	+ 2	21	15	do	do	do	Extensive necrosis; casts.	do	
837	146	+ 3	21	25	do	do	do	Very extensive necrosis; calcification; casts.	do	
838	107	+ 7	21	30	do	do	do	Extensive necrosis; casts.	do	
840	98	+ 7	21	40	do	do	do	Moderate necrosis; casts.	do	
851	122	0	19	13	do	4 days	Died	Extreme necrosis; calcification; casts.	Congestion	

All of the rats lived 20 hours or longer; 90 per cent showed kidney necrosis. Eighty-six per cent of the rats lived to be sacrificed.

TABLE 33.—*Neoarsphenamine—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[80 c. c. 1/100 arsenic equivalent solution, or 315 mg. neoarsphenamine per kilo body weight.]

[Room temperature 17.5° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
825	83	+ 7	19	5	Slight	5 days	Killed	Very extensive necrosis; casts.	No definite change.	
826	88	+ 2	19	11	...do	...do	...do	Extreme necrosis; calcification; casts.	.....do	Adrenals hemorrhagic.
827	83	+ 1	19	16	...do	...do	...do	Extensive necrosis; casts.	.....do	
828	93	+ 1	19	21	...do	...do	...do	Extensive necrosis; calcification; casts.	.....do	
830	85	+ 1	19	26	...do	...do	...do	Extensive necrosis; casts.	.....do	Few small liver abscesses.
833	76	+13	19	33	...do	...do	...do	Moderate necrosis.	.....do	
834	88	+ 7	19	38	...do	...do	...do	Extensive necrosis; casts.	.....do	
839	90	+11	21	35	...do	...do	...do	.....do	.....do	
841	87	+ 3	20	35	...do	...do	...do	Extensive necrosis; calcification; casts.	.....do	
842	88	+ 6	20	39	...do	...do	...do	Extensive necrosis; casts.	.....do	
844	99	+ 1	22	44	...do	...do	...do	Extensive necrosis; calcification; casts.	.....do	
850	80	+ 5	19	5	...do	...do	...do	Extensive necrosis; casts.	.....do	
852	90	+ 2	19	20	...do	3 days	Died	Extreme necrosis; calcification; casts.	Congestion	
853	93	0	20	25	...do	5 days	Killed	Extensive necrosis; casts.	No definite change.	
854	81	+ 9	20	30	...do	...do	...do	Extensive necrosis; calcification; casts.	.....do	

All of the rats lived three days or longer and showed kidney necrosis. Ninety-three per cent lived to be sacrificed.

TABLE 34.—*Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[2 c. c. 1/100 arsenic equivalent solution or 5.4 mg. "arsenoxide" per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
867	76	+ 5	19	34	Slight	2 days	Killed	No definite change.	No definite change.	
868	79	+16	19	1	do.	do.	do.	do.	do.	
869	76	+18	19	3	do.	do.	do.	do.	do.	
874	66	+ 6	19	26	do.	do.	do.	do.	do.	
875	84	+17	19	28	do.	do.	do.	do.	do.	
876	87	+26	19	30	do.	do.	do.	do.	do.	
877	72	+11	19	31	do.	do.	do.	do.	do.	Many small liver abscesses.
878	70	+21	19	33	do.	do.	do.	do.	do.	
879	90	+23	19	13	do.	do.	do.	do.	do.	Do.
880	71	+ 1	19	15	do.	do.	do.	do.	do.	Do.
881	70	+29	19	17	do.	do.	do.	do.	do.	
882	83	+11	19	19	do.	do.	do.	do.	do.	
883	65	+20	19	21	do.	do.	do.	do.	do.	
884	67	+15	19	23	do.	do.	do.	do.	do.	

All of the rats lived to be sacrificed; none showed kidney or liver necrosis.

TABLE 35.—*Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[4 c. c. 1/100 arsenic equivalent solution or 10.7 mg. "arsenoxide" per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
855	78	+18	19	5	Slight	2 days	Killed	No definite change.	No definite change.	
856	70	+33	19	10	do	do	do	do	do	
857	73	+14	19	11	do	do	do	do	do	Few lung abscesses.
858	77	+17	19	14	do	do	do	do	do	
859	84	+10	19	16	do	do	do	do	do	
860	102	+ 4	19	19	do	do	do	do	do	
861	82	+22	19	21	do	do	do	do	do	
862	84	+23	19	23	do	do	do	do	do	
863	84	+21	19	25	do	do	do	Slight necrosis.	do	Liver contains tapeworm cyst.
864	82	+15	19	28	do	do	do	No definite change.	do	
865	95	+17	19	29	do	do	do	do	do	
866	74	+18	19	31	do	do	do	do	do	
870	103	+ 9	19	5	do	do	do	do	do	
871	89	+15	19	8	do	do	do	do	do	
872	80	+14	19	10	do	do	do	do	do	

All of the rats lived to be sacrificed; 7 per cent showed kidney necrosis.

TABLE 36.—*Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[6 c. c. 1/100 arsenic equivalent solution or 16 mg. "arsenoxide" per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
900	62	− 2	23	1	Slight	2 days	Killed	No definite change.	No definite change.	
901	62	+ 3	23	3	do	do	do	Slight necrosis	do	
902	68	+ 6	23	8	do	do	do	No definite change.	do	
903	66	+ 6	23	10	do	do	do	do	do	
904	63	+ 5	23	15	do	do	do	do	do	
905	97	+13	23	17	do	do	do	Slight necrosis	do	
906	97	+ 3	23	21	do	do	do	do	do	Lung abscesses.
907	68	− 4	23	25	do	do	do	No definite change.	do	
908	86	− 1	23	28	do	do	do	do	do	Liver contains tapeworm cysts.
911	66	+ 9	21	30	Moderate	do	do	Slight necrosis	do	
912	65	+ 2	21	35	do	do	do	do	do	
913	58	0	21	33	do	18 hours	Died	Congestion; cloudy swelling.	Congestion	
914	72	−11	21	24	do	2 days	Killed	No definite change.	No definite change.	

All of the rats lived 18 hours or longer; 38 per cent showed kidney necrosis; 92 per cent of the animals lived to be sacrificed.

TABLE 37.—*Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt)—Rats injected intravenously after six days on bread, rolled oats and milk.*

[8 c. c. 1/100 arsenic equivalent solution or 21.4 mg. "arsenoxide" per kilo body weight.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
885	104	+15	19	22	Severe	2 days	Killed	Cloudy swelling; congestion.	No definite change.	
886	102	+18	19	7	do	do	do	Slight necrosis; congestion.	do	
887	104	+ 6	19	14	do	do	do	Cloudy swelling; congestion.	Congestion	
888	116	+ 8	19	17	do	do	do	Slight necrosis; congestion.	No definite change.	
889	122	+ 7	19	3	do	do	do	do	do	
890	100	+ 5	19	27	do	do	do	do	do	Lung abscesses.
891	81	− 1	19	32	do	do	do	Moderate necrosis; casts.	do	Do.
892	94	+ 6	22	5	do	do	do	do	do	
893	96	+ 2	22	20	do	do	do	Extensive necrosis; casts.	Many mitoses	Do.
894	92	+ 7	22	15	do	do	do	Moderate necrosis; casts.	No definite change.	
895	142	− 1	22	2	do	do	do	Extensive necrosis; casts.	do	
896	101	+11	22	10	do	do	do	do	do	Few small liver abscesses.
897	82	+ 2	22	17	do	do	do	Moderate necrosis; casts.	do	
898	132	− 2	22	27	do	do	do	Slight necrosis	do	
899	74	− 5	22	31	do	17 hours	Died	Cloudy swelling; congestion.	do	Many small liver abscesses.

All of the rats lived 17 hours or longer; 80 per cent showed kidney necrosis; 93 per cent of the animals lived to be sacrificed.

TABLE 38. *-Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt)—Rats injected intravenously after six days on bread, rolled oats, and milk.*

[10 c. c. 1/100 arsenic equivalent solution or 26.8 mg. "arsenoxide" per kilo body weight.]

[Room temperature 18.5° C.]

Rat.	Initial weight.	Weight loss or gain.	Fast before injection.	Age of alkaline solution.	Clinical reaction.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Per ct.*	*Hours.*	*Mins.*						
925	102	+5	19	11	Severe....	2 days.....	Killed.....	Moderate necrosis; casts.	No definite change.	Pregnant. Lungs edematous.
931	148	−4	19	14	...do.......	3½ hours...	Died......	Cloudy swelling; congestion; interstitial hemorrhages; casts.	Congestion........	Acute lung picture; pleural fluid increased.
932	130	−5	19	19	...do.......	11 hours...	...do.......	Congestion; cloudy swelling; interstitial hemorrhages.	.....do.............	Acute lung picture; pleural fluid increased; spleen slightly congested.
934	160	+9	22	4	...do.......	5½ hours...	...do.......	Congestion; interstitial hemorrhages.	Congestion; fat++	Do.
935	102	+1	22	8	...do.......	2 days.....	Killed.....	Extensive necrosis; casts.	Many mitoses.....	Lung abscesses.
936	150	+3	22	12	...do.......	...do.......	...do.......	.....do.............	Few mitoses; fat droplets+.	
949	150	+1	19	19	...do.......	1½ hours...	Died......	Slight congestion..	Congestion........	Lungs slightly edematous; pleural fluid increased; tapeworm cyst in liver.
950	116	+14	19	24	...do.......	2 days.....	Killed.....	Moderate necrosis.	No definite change.	
951	162	+1	19	30	...do.......	6¾ hours...	Died......	Congestion; interstitial hemorrhages.	Congestion........	Acute lung picture; pleural fluid increased; many small liver abscesses.
953	110	−6	19	5	...do.......	2 days.....	Killed.....	Moderate necrosis; casts.	Many mitoses.....	
954	98	+1	19	8	...do.......	...do.......	...do.......	Extensive necrosis; casts.	Few mitoses......	Lung abscesses; tapeworm cyst in liver.

55 per cent of the rats lived to be sacrificed; all of these showed kidney necrosis. The animals that died acutely showed distention, congestion, and edema of lungs. As a rule the pleural fluid was markedly increased.

TABLE 39.—*Para-oxy-meta-amino-phenyl-arsenoxide (sodium salt) intramuscularly.*

[10 c. c. 1/100 arsenic equivalent solution or 26.8 mg. "arsenoxide" per kilo body weight.]

Rat.	Weight.	Age of alkaline solution.	Length of life.	Termination.	Kidney.	Liver.	Remarks.
	Gm.	*Mins.*					
921	160	21	5 days	Killed	Extensive necrosis.	No definite change.	Muscle necrosis at site of injection; accumulation of polyblasts.
923	106	20	...do	...do	No definite change.	...do	Muscle necrosis at site of injection.
[20 c. c. 1/100 arsenic equivalent solution or 54 mg. "arsenoxide" per kilo body weight.]							
922	144	24	5 days	Died	Extreme necrosis; casts.	Congestion; otherwise no change.	Extensive muscle necrosis and edema and accumulation of polyblasts at site of injection. Lungs congested and consolidated in areas. Liver contains tapeworm cyst.
924	198	15	4 hours	...do	Congestion	Congestion	Site of injection swollen and extensively edematous; some accumulation of leucocytes; lungs congested; no edema.
[30 c. c. 1/100 arsenic equivalent solution or 80 mg. "arsenoxide" per kilo body weight.]							
915	100	5	7 hours	Died	No definite change.	No definite change.	Site of injection swollen; lungs normal; small intestine slightly congested.
920	92	17	...do	...do	Congestion	Congestion	Lungs congested; no edema.
[40 c. c. 1/100 arsenic equivalent solution or 107 mg. "arsenoxide" per kilo body weight.]							
917	130	12	7 hours	Died	No definite change.	No definite change.	Site of injection swollen.
918	108	7	...do	...do	......do	......do	Do
[50 c. c. 1/100 arsenic equivalent solution or 134 mg. "arsenoxide" per kilo body weight.]							
916	108	10	1½ hours	Died	No definite change.	Congestion	Lungs normal; no increase in pleural fluid.
919	144	2	1 hour	...do	......do	Slight congestion	Mucosa of small intestine congested; lungs normal.

It is seen from the above table that p-oxy-m-amino-phenyl-arsenoxide is rapidly absorbed when given intramuscularly and that it ultimately damages the kidneys. Extensive muscle necrosis is produced at the site of the injection with edema and accumulation of polyblasts.

HYGIENIC LABORATORY BULLETINS OF THE PUBLIC HEALTH SERVICE.

The Hygienic Laboratory was established in New York, at the Marine Hospital on Staten Island, August, 1887. It was transferred to Washington, with quarters in the Butler Building, June 11, 1891, and a new laboratory building, located in Washington, was authorized by act of Congress March 3, 1901.

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